

Role of REMS fracture risk prediction within the DVO-based fracture risk framework: a retrospective observational study

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Abstract

Background

The 2023 German DVO guidelines introduced a risk-adapted osteoporosis management based on 3-year fracture risk, integrating DXA-T-scores with demographic, anthropometric and clinical risk factors. Within this framework, Radiofrequency Echographic Multi-Spectrometry (REMS), a radiation-free ultrasound-based technology providing densitometric parameters, Fragility Score (FS), and 5-year fracture risk stratification, may offer complementary skeletal information relevant to DVO-based assessment.

Aim

To compare DXA-DVO 2023 risk categories with exploratory REMS-DVO-equivalent categories, and to evaluate the relationships of REMS-DVO categories with FS and REMS 5-year fracture risk classes.

Methods

This retrospective observational study included 256 patients who underwent paired DXA and REMS examinations ($n = 128$ per site). DVO 2023 risk categories were calculated using DXA-T-scores and compared with estimates obtained by REMS-T-scores while keeping all other factors unchanged. Agreement was assessed using percentage agreement and weighted Cohen's kappa before and after applying a ± 0.3 tolerance at T-score thresholds. Internal coherence with FS and 5-year fracture risk categories was evaluated across DVO categories by Kruskal-Wallis followed by Wilcoxon tests with false discovery rate correction.

Results

DXA-based and REMS-substituted DVO categories showed high agreement at both sites: 81.2% ($\kappa = 0.84$) at the femur and 80.5% ($\kappa = 0.85$) at the spine. After ± 0.3 tolerance, agreement increased to 86.7% ($\kappa = 0.87$) and 83.6% ($\kappa = 0.87$), respectively. FS progressively increased across higher DVO risk categories, while REMS 5-year fracture risk classes shifted toward higher-risk categories with increasing DVO thresholds.

Conclusions

REMS-derived parameters showed substantial coherence with DVO risk groups, supporting REMS technology as a valuable tool allowing a timely indication for intervention and preventive strategies.

Introduction

Osteoporosis is defined as a multifactorial systemic skeletal disease characterized by low bone mass and microstructural deterioration of bone tissue, leading to increased bone fragility and a higher incidence of fractures [1]. The main clinical manifestation of osteoporosis is a fragility fracture. Currently, it is estimated that approximately 6 million people are affected by osteoporosis in Germany and its clinical burden is rising [2]. Fracture incidence has increased over the period from 2009 to 2019 by 15% for all skeletal sites, by 23% for femoral neck and by 24% for pertrochanteric fractures [3]. These fracture events, especially those occurring at spine and hip, are associated with significantly elevated morbidity and mortality rates, as well as a substantial socioeconomic impact [4]. Despite the availability of diagnostic tools and therapeutic treatments, a gap still exists, with 71% of the eligible German population necessitating a more proactive and structured approach to personalized care [2].

In response to these challenges, the German-speaking Scientific Societies for Osteology (DVO, Association of Scientific Medical Societies in Germany, whose guidelines are registered in the AWMF guideline register) updated the S3 guidelines in 2023 with a significant paradigm shift towards a more individualized and risk-adapted medicine [5]. The most important updates include the transition from a 10-year fracture risk prediction model to a shorter 3-year assessment period [5]. The introduction of a shorter timeframe allows for a more clinically oriented estimation and better communicability of imminent fracture risk and reduces the confounding influence of mortality, which is particularly relevant in the elderly population [2]. The calculation is obtained by the integration of dual-energy X-ray absorptiometry (DXA) derived T-score along with anthropometric, demographic and clinical risk factors [5]. The update has also revised the therapeutic framework into a three-staged threshold system: a risk corridor between 3% to < 5% is established to allow for early intervention in patients with strong or irreversible risk factors, a specific pharmacological therapy is strongly recommended between 5% to < 10% risk, while patients exceeding 10% are urgently prioritized for initial osteoanabolic therapy [2]. By integrating these nuanced risk assessments with interdisciplinary collaboration, the DVO 2023 guidelines aim to close the current treatment gap and optimize long-term outcomes.

Radiofrequency Echographic Multi-Spectrometry (REMS) is an ultrasound-based, radiation-free and non-invasive technology for the assessment of bone densitometry. The technology analyzes the native radiofrequency signals acquired from echographic scans at lumbar spine and femur using a dedicated spectral algorithm that compares the patient-specific signals to proprietary spectral models derived from age- and sex-matched healthy populations [6, 7]. The result is an estimate of bone mineral density (BMD) and the derived parameters (T-score and Z-score) reflecting the properties of the bone. In addition, REMS technology also provides a proprietary parameter reflecting bone quality known as Fragility Score (FS), which is able to capture microarchitectural information not covered by BMD through a comparison of the ultrasound signals with spectral characteristics of fractured and non-fractured patients [8, 9]. Fragility Score provides additional insights into skeletal fragility and has shown a higher discriminative ability in identifying individuals at high risk of fracture compared with both DXA- and REMS-derived T-score [10]. In addition, by integrating quantitative information related to bone quantity (T-score) with quantitative information related to bone quality (FS), REMS technology also provides a short-term fracture risk

stratification in 7 risk classes (named R1 to R7) along with a probability of sustaining a fracture within 5 years.

Although REMS showed diagnostic agreement with DXA [11, 12], an ability to avoid clinically relevant artefacts that may lead to BMD overestimation [13, 14] and high effectiveness for short-term bone monitoring [15–17], its potential role within country-specific fracture risk frameworks, such as the German DVO 2023 risk algorithm, remains unexplored.

Therefore, this study aimed to compare fracture risk categories derived from the 2023 DVO risk calculator using DXA-derived T-scores with corresponding DVO-equivalent categories obtained by replacing DXA T-scores with REMS-derived T-scores. Subsequently, internal coherence between REMS German DVO categories and REMS FS and 5-year fracture risk stratification was explored. This approach was designed to assess whether REMS-derived densitometric parameters may provide comparable risk stratification within a DVO-based clinical decision-making framework.

Materials and methods

Patients and measurements

The study included patients who met the following eligibility criteria: Caucasian ethnicity, postmenopausal women and men, aged 50–80 years, medical prescriptions for spinal or femoral DXA examinations and absence of any significant ambulation difficulties. All patients had provided written informed consent for the use of their anonymized clinical data for research and quality management purposes.

According to the study protocol, patients underwent a DXA and a REMS scan examination at the same anatomical site (lumbar spine or femoral neck).

Examinations

DXA scans were conducted using a Discovery W scanner (Hologic, Waltham, MA, USA) following standard clinical procedures. For spine investigations, the patient's hips and knees were both flexed at 90°. During femoral scans, the patient's femur was positioned straight on the table, with the shaft parallel to the vertical edge of the image and internally rotated by 15–25°. Medical reports generated by the scanner were anonymized and checked for quality by three independent operators prior to being used for statistical analysis.

REMS scans were performed using an EchoStation device (Echolight S.p.a., Lecce, Italy) equipped with a convex transducer operating at a nominal frequency of 3.5 MHz, following the manufacturer's instructions. The acquisitions were performed according to procedures described in previously published work [6, 7]. Briefly, for lumbar spine examinations, the echographic transducer was positioned

trans-abdominally under the sternum to initially visualize the L1 vertebra. The probe was then moved from L1 to L4, following the audible instructions from the EchoStudio software (v2.2.2, Echolight S.p.a., Lecce, Italy) during an 80 s acquisition. Femoral neck scans were performed by positioning the echographic transducer parallel to the head–neck axis of the femur to visualize the head, neck and trochanter. Once the target interfaces were identified, the probe was held for 40 s according to the indications provided by the device. All REMS acquisitions were performed by a single experienced operator who had received the specific training program according to the guidelines of the device manufacturer and had at least 3 months (and more than 60 patients) of prior experience with REMS acquisitions. At the time of REMS acquisition and quality assessment, operators were blinded to the corresponding DXA results. All data were collected and documented by an independent, blinded physician who was not involved in the treatment of the patients.

German DVO risk calculation

The 2023 German DVO fracture risk categories ($< 3\%$, 3% to $< 5\%$, 5% to $< 10\%$ and $\geq 10\%$) were estimated using the DVO algorithm to calculate the individual risk threshold, controlled by a web-based calculator for training and quality control available at <https://osteoporose.bvou.net/>, which provides a digital implementation of the DVO 2023 risk assessment framework [18]. The following variables were entered into the calculator: sex, age category, densitometric T-score and clinical risk factors. Age was entered from 50 years onward in 5-year intervals. For the standard DVO calculation, the DXA-derived T-score was used. For the exploratory REMS-substituted calculation, the corresponding REMS-derived T-score was entered while keeping sex, age and clinical risk factors unchanged. T-score values were entered in 0.5-unit intervals.

The clinical risk factors considered in the calculation were those systematically available in the clinical records, and included: body mass index (BMI) $< 20 \text{ kg/m}^2$, previous vertebral fracture(s), parental history of hip fracture, current smoking of > 10 cigarettes/day, oral glucocorticoid therapy with prednisolone or equivalent, rheumatoid arthritis, type 1 or type 2 diabetes mellitus, alcohol consumption $> 50 \text{ g/day}$ and risk of falling. When more than one clinical risk factor was present, risk factors were selected according to the DVO 2023 rules for risk-factor grouping and prioritization.

Parameters

For both DXA and REMS examinations, BMD (measured in g/cm^2) and T-score values were included in the subsequent statistical analysis. According to the World Health Organization (WHO), osteoporosis is defined by a T-score ≤ -2.5 at lumbar spine, femoral neck or total hip [19].

REMS-measured Fragility Score is a dimensionless parameter, independent of BMD, that is automatically calculated by comparison of the native radiofrequency signals reflected by the bone interface with reference spectral models previously built from fractured and non-fractured patients [8, 9]. From this

comparison, the system automatically provides a quantitative estimation ranging from 0 (maximum similarity with the healthy model) to 100 (maximum similarity with the fractured model). Bone quality is therefore classified as normal when FS falls into the green code, as reduced when FS falls into the yellow code, or as low when FS falls into the red code.

The REMS short-term 5-year fracture risk stratification is obtained by combining the 3 diagnostic ranges of REMS T-score with the 3 classes of FS. If the REMS scan is performed at the lumbar spine, the combination generates the risk for major osteoporotic fractures (MOF). If the REMS scan is performed at the femoral neck, the combination generates the risk for hip fractures (HF). The classification consists of 7 risk classes, named R1 (lowest risk) to R7 (highest risk), along with a specific, increasing probability of developing a MOF or HF within 5 years.

Statistical analysis

Descriptive statistics were used to summarize the demographic, anthropometric, clinical and densitometric characteristics of the study population. Continuous variables were reported as median and interquartile range (Q1–Q3), whereas categorical variables were reported as absolute frequencies and percentages. Analyses were performed separately for patients who underwent femoral and spinal acquisitions. The level of agreement between DVO 2023 risk categories calculated using DXA-derived T-scores and the corresponding REMS-substituted DVO-equivalent risk categories was assessed using percentage agreement and weighted Cohen's kappa coefficient with 95% confidence intervals, using weights based on the distance from the diagonal [20]. The strength of agreement was interpreted according to the Landis and Koch criteria [21]. To correctly account for borderline cases, the level of agreement between DVO 2023 risk categories using DXA-derived T-scores and the corresponding REMS-substituted DVO-equivalent risk categories was also calculated after applying a tolerance of ± 0.3 to the T-score thresholds (T-score = -1.0 and T-score = -2.5), in line with previous REMS-DXA diagnostic agreement studies [11].

Fragility Score values were compared across DVO 2023 risk categories ($< 3\%$, 3% to $< 5\%$, 5% to $< 10\%$, and $\geq 10\%$) using the Kruskal-Wallis rank-sum test. When a significant overall difference was detected, post-hoc pairwise comparisons were performed using Wilcoxon rank-sum tests with false discovery rate (FDR) correction for multiple testing.

All analyses and graphs were produced using R statistical software (version 4.5.2) [22]. A p-value < 0.05 was always considered statistically significant.

Results

Patients' characteristics

A total of 128 patients met the inclusion criteria and were recruited; this group underwent a DXA and a REMS scan of the femur, and the same group underwent a DXA and a REMS scan of the spine.

The demographic, anthropometric, clinical and densitometric characteristics of the two study cohorts are reported in Table 1.

Table 1. Anthropometric, demographic, clinical and densitometric data of patients recruited who underwent DXA and REMS scans at femur (n = 128) or spine (n = 128). Continuous variables are reported as median (first and third quartile); categorical variables are reported as counts and percentages.

Patients who underwent femoral acquisitions (n = 128)	
Age (years)	
Median (Q1, Q3)	61.00 (53.50, 68.00)
Min, Max	50.00, 86.00
≤ 60	59/128, 46.1%
> 60	69/128, 53.9%
Sex	
F	86/128, 67.2%
M	42/128, 32.8%
Weight (kg)	
Median (Q1, Q3)	71.00 (60.00, 81.50)
Min, Max	42.00, 124.00
Height (cm)	
Median (Q1, Q3)	165.00 (159.50, 172.00)
Min, Max	144.00, 192.00
BMI (kg/m²)	
Median (Q1, Q3)	25.66 (23.56, 29.32)
Min, Max	17.26, 38.27
Underweight (< 18.5 kg/m ²)	3/128, 2.3%
Normal (18.5 – 24.9 kg/m ²)	52/128, 40.6%
Overweight (25.0 – 29.9 kg/m ²)	45/128, 35.2%
Obesity (≥ 30.0 kg/m ²)	28/128, 21.9%
Femoral DXA BMD (g/cm²)	
Median (Q1, Q3)	0.715 (0.646, 0.798)
Min, Max	0.479, 1.196
Femoral DXA T-score	
Median (Q1, Q3)	-1.3 (-1.9, -0.7)
Min, Max	-3.3, 1.9
Femoral REMS BMD (g/cm²)	
Median (Q1, Q3)	0.700 (0.610, 0.780)

Min, Max	0.440, 1.010
Femoral REMS T-score	
Median (Q1, Q3)	-1.6 (-2.2, -0.9)
Min, Max	-3.7, 1.5
Fragility Score	
Median (Q1, Q3)	22.7 (15.6, 35.3)
Min, Max	10.3, 85.3
REMS Fracture Risk (%)	
R1: ≤ 0.1	41/128, 32.0%
R2:]0.1-0.4]	1/128, 0.8%
R3:]0.4-0.8]	44/128, 34.4%
R4:]0.8-1.5]	11/128, 8.6%
R5:]1.5-3.0]	20/128, 15.6%
R6:]3.0-5.0]	3/128, 2.3%
R7: > 5.0%	8/128, 6.3%
Previous vertebral fracture(s)	68/128, 53.1%
Parental history of hip fracture	19/128, 14.8%
Current smoking (> 10 cigarettes/day)	2/128, 1.6%
Prednisolone or equivalents	5/128, 3.9%
Rheumatoid arthritis	4/128, 3.1%
Diabetes mellitus type I/II	27/128, 21.1%
Alcohol (> 50 g/day)	8/128, 6.3%
German DVO 2023 (T-score-DXA)	
< 3%	64/128, 50.0%
3% to < 5%	27/128, 21.1%
5% to < 10%	19/128, 14.8%
≥ 10%	18/128, 14.1%
German DVO 2023 (T-score-REMS)	
< 3%	52/128, 40.6%
3%to < 5%	32/128, 25.0%

5% to <10%	21/128, 16.4%
≥ 10%	23/128, 18.0%
Patients who underwent spine acquisitions (n = 128)	
Age (years)	
Median (Q1, Q3)	60.00 (52.00, 67.50)
Min, Max	50.00, 85.00
≤ 60	65/128, 50.8%
> 60	63/128, 49.2%
Sex	
F	76/128, 59.4%
M	52/128, 40.6%
Weight (kg)	
Median (Q1, Q3)	70.00 (60.00, 80.50)
Min, Max	45.00, 105.00
Height (cm)	
Median (Q1, Q3)	166.00 (159.00, 172.50)
Min, Max	143.00, 190.00
BMI (kg/m²)	
Median (Q1, Q3)	25.35 (22.67, 28.44)
Min, Max	18.83, 36.76
Underweight (< 18.5 kg/m ²)	0/128, 0%
Normal (18.5 – 24.9 kg/m ²)	61/128, 47.7%
Overweight (25.0 – 29.9 kg/m ²)	44/128, 34.4%
Obesity (≥ 30.0 kg/m ²)	23/128, 18.0%
Lumbar DXA BMD (g/cm²)	
Median (Q1, Q3)	0.906 (0.822, 1.023)
Min, Max	0.471, 1.280
Lumbar DXA T-score	
Median (Q1, Q3)	-1.4 (-2.2, -0.4)
Min, Max	-5.6, 1.9

Lumbar REMS BMD (g/cm²)	
Median (Q1, Q3)	0.880 (0.810, 0.950)
Min, Max	0.660, 1.180
Lumbar REMS T-score	
Median (Q1, Q3)	-1.7 (-2.3, -1.1)
Min, Max	-3.5, 1.3
Fragility Score	
Median (Q1, Q3)	27.0 (23.0, 36.5)
Min, Max	18.9, 79.2
REMS Fracture Risk	
R1: ≤ 0.5	26/128, 20.3%
R2:]0.5-1.0]	2/128, 1.6%
R3:]1.0-2.0]	69/128, 53.9%
R4:]2.0-3.5]	7/128, 5.5%
R5: [3.5-6.0]	17/128, 13.3%
R6: [6.0-10.0]	4/128, 3.1%
R7: > 10.0	3/128, 2.3%
Previous vertebral fracture(s)	62/128, 48.4%
Parental history of hip fracture	11/128, 8.6%
Current smoking (> 10 cigarettes/day)	19/128, 14.8%
Prednisolone or equivalents	10/128, 7.8%
Rheumatoid arthritis	6/128, 4.7%
Diabetes mellitus type I/II	26/128, 20.3%
Alcohol (> 50 g/day)	9/128, 7.0%
German DVO 2023 (T-score DXA)	
< 3%	61/128, 47.7%
3% to <5%	20/128, 15.6%
5% < 10%	28/128, 21.9%
≥ 10%	19/128, 14.8%
German DVO 2023 (T-score REMS)	

< 3%	56/128, 43.8%
3%to < 5%	21/128, 16.4%
5% to< 10%	27/128, 21.1%
≥ 10%	24/128, 18.8%

German DVO DXA-T-score vs. German DVO REMS-T-score

Table 2 shows the agreement between German DVO 2023 risk categories calculated using DXA T-score and the corresponding categories calculated using REMS T-score, both before and after applying a ± 0.3 tolerance at the T-score thresholds, separately for femur and spine.

At the femoral site, the highest proportion of patients in each DXA-based DVO category (<3%, 3% to <5%, 5% to <10%, and $\geq 10\%$) was classified into the corresponding REMS-substituted DVO category, and this remained consistent also after the ± 0.3 tolerance at T-score thresholds. Complete agreement was observed in the highest-risk category ($\geq 10\%$) in both cases. Notably, REMS-substituted DVO classification assigned patients to a lower risk category than DXA-based classification only among those classified as 5% to <10% by DXA, in both cases. Overall, the two classifications showed substantial agreement (81.2%, with a weighted Cohen's $k = 0.84$) that further increased when considering the ± 0.3 tolerance (percentage agreement: 86.7%; weighted Cohen's $k = 0.87$).

At the spinal site, a similar pattern was observed both before and after applying the ± 0.3 tolerance at T-score thresholds: for each DXA-based DVO category, the highest proportion of patients was classified into the corresponding REMS-substituted DVO category. Overall, the percentage agreement was 80.5% (weighted Cohen's $k = 0.85$), increasing to 83.6% (weighted Cohen's $k = 0.87$) after applying the tolerance.

Table 2. Distribution of German DVO 2023 risk categories (<3%, 3% to <5%, 5% to <10%, $\geq 10\%$) calculated using DXA T-score and REMS-substituted DVO-equivalent risk (<3%, 3% to <5%, 5% to <10%, $\geq 10\%$) before and after applying the ± 0.3 tolerance at T-score thresholds at both femur and spine. CI: confidence interval.

DXA-DVO categories (femur), before the ± 0.3 tolerance

DXA-DVO category	< 3%	3% to < 5%	5% to < 10%	$\geq 10\%$
< 3%	52/64 (81.3%)	7/64 (10.9%)	4/64 (6.3%)	1/64 (1.5%)
3% to < 5%	0/27 (0%)	21/27 (77.8%)	4/27 (14.8%)	2/27 (7.4%)
5% to < 10%	0/19 (0%)	4/19 (21.1%)	13/19 (68.4%)	2/19 (10.5%)
$\geq 10\%$	0/18 (0%)	0/18 (0%)	0/18 (0%)	18/18 (100%)

Weighted Cohen's *k*: 0.84, 95% CI: 0.76–0.93. Degree of agreement: Almost perfect [21].

Percentage of agreement: 81.2%.

DXA-DVO categories (femur), after the ± 0.3 tolerance

DXA-DVO category	< 3%	3% to < 5%	5% to < 10%	$\geq 10\%$
< 3%	52/61 (85.2%)	4/61 (6.6%)	4/61 (6.6%)	1/61 (1.6%)
3% to < 5%	0/28 (0%)	25/28 (89.3%)	1/28 (3.6%)	2/28 (7.1%)
5% to < 10%	0/21 (0%)	3/21 (14.3%)	16/21 (76.2%)	2/21 (9.5%)
$\geq 10\%$	0/18 (0%)	0/18 (0%)	0/18 (0%)	18/18 (100%)

Weighted Cohen's *k*: 0.87, 95% CI: 0.78–0.95. Degree of agreement: Almost perfect [21].

Percentage of agreement: 86.7%.

DXA-DVO categories (spine), before the ± 0.3 tolerance

DXA-DVO category	< 3%	3% to < 5%	5% to < 10%	$\geq 10\%$
< 3%	53/61 (86.9%)	5/61 (8.2%)	2/61 (3.3%)	1/61 (1.6%)
3% to < 5%	1/20 (5.0%)	15/20 (75.0%)	4/20 (20.0%)	0/20 (0%)
5% to < 10%	1/28 (3.6%)	1/28 (3.6%)	19/28 (67.8%)	7/28 (25%)
$\geq 10\%$	1/19 (5.3%)	0/19 (0%)	2/19 (10.5%)	16/19 (84.2%)

Weighted Cohen's *k*: 0.85, 95% CI: 0.77–0.94. Degree of agreement: Almost perfect [21].

Percentage of agreement: 80.5%.

DXA-DVO categories (spine), after the ± 0.3 tolerance

DXA-DVO category	< 3%	3% to < 5%	5% to < 10%	$\geq 10\%$
< 3%	53/61 (86.9%)	5/61 (8.2%)	2/61 (3.3%)	1/61 (1.6%)
3% to < 5%	0/19 (0%)	16/19 (84.2%)	3/19 (15.8%)	0/19 (0%)
5% to < 10%	1/29 (3.4%)	1/29 (3.4%)	21/29 (72.5%)	6/29 (20.7%)
$\geq 10\%$	1/19 (5.3%)	0/19 (0%)	1/19 (5.3%)	17/19 (89.4%)

Weighted Cohen's *k*: 0.87, 95% CI: 0.78–0.95. Degree of agreement: Almost perfect [21].

Percentage of agreement: 83.6%.

German DVO vs. Fragility Score

Figure 1 shows the distribution of Fragility Score values across German DVO thresholds for femoral (a) and spine (b) acquisitions.

For femoral acquisitions, FS differed significantly across the DVO 2023 threshold groups (<3%, 3% to <5%, 5% to <10%, ≥10%; $p < 0.001$). Median FS increased stepwise with higher DVO thresholds, from 14.6 (Q1–Q3: 12.7–21.1) in the <3% group to 22.9 (19.5–29.9) in the 3% to <5% group, 33.4 (25.8–42.6) in the 5% to <10% group, and 55.5 (34.7–66.1) in the ≥10% group. Table 3 summarizes the median femoral FS values with post-hoc pairwise comparisons using Wilcoxon tests with FDR correction, which showed significant differences between all group pairs.

For spine acquisitions, FS values also differed significantly across the DVO 2023 threshold groups (<3%, 3% to <5%, 5% to <10%, ≥10%; $p < 0.001$). Median FS increased with higher DVO thresholds, from 24.1 (Q1–Q3: 21.6–28.1) in the <3% group, to 27.3 (23.9–33.4) in the 3% to <5% group, 30.0 (24.8–41.7) in the 5% to <10% group, and 40.7 (28.5–56.6) in the ≥10% group. Table 3 summarizes the median spinal FS values with post-hoc pairwise comparisons, which showed significant differences for the following comparisons: <3% vs. 5% to <10%, <3% vs. ≥10%, 3% to <5% vs. ≥10%, and 5% to <10% vs. ≥10%.

Table 3. Distribution of Fragility Score values by DVO 2023 threshold categories (<3%, 3% to <5%, 5% to <10%, ≥10%) along with Wilcoxon test with false discovery rate (FDR) correction and related p-values at femoral and spinal sites.

Femoral acquisitions

REMS German DVO 2023 risk categories					p-value
	<3%	3% to <5%	5% to <10%	≥10%	
	n = 52	n = 32	n = 21	n = 23	
Fragility Score					<0.001
Median (Q1, Q3)	14.6 (12.7, 21.1)	22.9 (19.5, 29.9)	33.4 (25.8, 42.6)	55.5 (34.7, 66.1)	

Multiple comparisons' p-value (femoral)					
<3% vs. 3% to <5%	<3% vs. 5% to <10%	3% to <5% vs. 5% to <10%	<3% vs. ≥10%	3% to <5% vs. ≥10%	5% to <10% vs. ≥10%
<0.001	<0.001	0.011	<0.001	<0.001	0.003

Spinal acquisitions

REMS German DVO 2023 risk categories					p-value
<3%	3% to <5%	5% to <10%	≥10%		
n = 56	n = 21	n = 27	n = 24		
Fragility Score					<0.001
Median (Q1, Q3)	24.1 (21.6, 28.1)	27.3 (23.9, 33.4)	30.0 (24.8, 41.7)	40.7 (28.5, 56.6)	

Multiple comparisons' p-value (spinal)					
<3% vs. 3% to <5%	<3% vs. 5% to <10%	3% to <5% vs. 5% to <10%	<3% vs. ≥10%	3% to <5% vs. ≥10%	5% to <10% vs. ≥10%
0.074	0.001	0.198	<0.001	0.004	0.027

Kruskal-Wallis rank-sum test for the overall comparison; Wilcoxon test with FDR correction for pairwise comparisons.

German DVO vs. REMS 5-year fracture risk

Table 4 shows the distribution of 5-year REMS fracture risk categories (R1 to R7) across DVO 2023 threshold groups (<3%, 3% to <5%, 5% to <10%, ≥10%) for femoral and spinal acquisitions.

In the femoral cohort (n = 128), lower REMS fracture risk categories (R1 ≤ 0.1% and R3 0.4–0.8%) dominated the lower DVO thresholds, particularly in the <3% group, where half of individuals fell into R1 and one-third into R3. As the DVO threshold increased, there was a noticeable shift toward higher fracture risk categories. In the ≥10% DVO group, higher REMS risk categories became more prevalent, with R5 (1.5–3.0%) accounting for 34.8% and R7 (>5.0%) for 30.4% of cases, while the lowest risk

category (R1) was rare (4.3%). Overall, this pattern suggests a positive association between higher DVO 2023 thresholds and increasing REMS-estimated fracture risk.

Regarding the spinal cohort (n = 128), in the <3% DVO group fracture risk was predominantly low, with 42.9% classified as R1 (≤ 0.5) and 50.0% as R3 (1.0–2.0). As the DVO threshold increased, the proportion of individuals in higher fracture risk categories increased. Notably, in the $\geq 10\%$ DVO group, 37.5% of individuals were classified as R5 (3.5–6.0), 8.3% as R6 (6.0–10.0), and 12.5% as R7 (>10.0), whereas no individuals in the <3% DVO group were classified in the R6 or R7 REMS risk classes. Overall, the distribution shows a clear shift toward higher fracture risk categories with increasing DVO 2023 thresholds.

Table 4. Distribution of REMS 5-year fracture risk classes (R1–R7) across REMS-substituted DVO categories (<3%, 3% to <5%, 5% to <10%, $\geq 10\%$) at the femoral and spinal sites. Percentages are calculated within each DVO category. HF: hip fracture(s); MOF: major osteoporotic fracture(s).

Fracture risk for HF (femoral site)

	REMS German DVO 2023 risk categories			
	<3%	3% to <5%	5% to <10%	$\geq 10\%$
R1: ≤ 0.1	26 (50%)	10 (31.2%)	4 (19%)	1 (4.3%)
R2:]0.1 – 0.4]	0 (0%)	0 (0%)	1 (4.8%)	0 (0%)
R3:]0.4 – 0.8]	17 (32.7%)	16 (50%)	7 (33.3%)	4 (17.4%)
R4:]0.8 – 1.5]	3 (5.8%)	3 (9.4%)	3 (14.3%)	2 (8.7%)
R5:]1.5 – 3.0]	4 (7.7%)	2 (6.2%)	6 (28.6%)	8 (34.8%)
R6:]3.0 – 5.0]	2 (3.8%)	0 (0%)	0 (0%)	1 (4.3%)
R7: > 5.0	0 (0%)	1 (3.1%)	0 (0%)	7 (30.4%)
Total	52 (100%)	32 (100%)	21 (100%)	23 (100%)

Fracture risk for MOF (spinal site)

REMS German DVO 2023 risk categories				
	<3%	3% to <5%	5% to <10%	≥10%
R1: ≤ 0.5	24 (42.9%)	2 (9.5%)	0 (0%)	0 (0%)
R2: [0.5 – 1.0]	1 (1.8%)	0 (0%)	1 (3.7%)	0 (0%)
R3:]1.0 – 2.0]	28 (50.0%)	13 (61.9%)	21 (77.8%)	7 (29.2%)
R4:]2.0 – 3.5]	0 (0%)	0 (0%)	4 (14.8%)	3 (12.5%)
R5:]3.5 – 6.0]	3 (5.4%)	5 (23.8%)	0 (0%)	9 (37.5%)
R6:]6.0 – 10.0]	0 (0%)	1 (4.8%)	1 (3.7%)	2 (8.3%)
R7: > 10.0	0 (0%)	0 (0%)	0 (0%)	3 (12.5%)
Total	56 (100%)	21 (100%)	27 (100%)	24 (100%)

Discussion

Osteoporosis is a silent multifactorial disease whose main clinical manifestation is a fragility fracture [23]. The German-speaking Scientific Societies for Osteology updated the 2023 guidelines for the prediction of patients at high risk of fractures, including DXA T-score along with anthropometric, demographic and clinical risk factors [5]. In this retrospective observational study, the agreement between German DVO 2023 risk categories including DXA T-score and exploratory German DVO 2023 risk categories including REMS T-score was evaluated in a cohort of patients (n = 256) undergoing paired DXA and REMS densitometric acquisitions at femur (n = 128) or spine (n = 128). To further assess the role of REMS within a DVO-based clinical decision-making framework, the coherence between REMS-DVO and REMS FS and 5-year fracture risk was explored. The study demonstrated that REMS-substituted German DVO risk categories (< 3%, 3% to < 5%, 5% to < 10%, ≥ 10%) show substantial agreement with standard German DVO 2023 categories based on DXA T-score, and similar trends with REMS parameters for prediction of skeletal fragility (FS) and fracture risk (5-year fracture risk stratification).

Male and female patients eligible for German DVO 2023 risk prediction (aged 50 or older, and postmenopausal women) who underwent DXA and REMS examinations at the same reference anatomical site (femur or spine) were included, and related anthropometric, demographic, clinical and densitometric data were collected. The 2023 DVO update introduced a clinically oriented shift from a 10-year fracture risk model to a shorter 3-year fracture risk model integrating densitometric, anthropometric, demographic and clinical risk factors, with therapeutic thresholds defined at 3% to < 5%, 5% to < 10% and ≥ 10% [5, 24]. In this context, the risk classification is not based on densitometric values alone (T-score) but integrates sex, age, BMI and other clinical risk factors. The observed level of agreement between DXA-based and REMS-based German DVO categories is clinically relevant. At the femoral site, the highest proportion of REMS-DVO classifications overlapped with the corresponding DXA-DVO category across all DVO thresholds, with complete agreement in the highest-risk category (≥ 10%). A similar

pattern was observed at the spine. Overall, the two reference anatomical sites showed high percentages of agreement (81.2% and 80.5% at femur and spine, respectively), with an almost perfect strength of agreement (weighted Cohen's $k = 0.84$ and 0.85 at femur and spine, respectively).

Notably, most discordant cases were reclassified into adjacent categories, suggesting that differences between the two approaches were generally limited rather than widely divergent. To correctly account for borderline cases potentially affected by small differences around the T-score thresholds, agreement was recalculated after applying a ± 0.3 tolerance at T-score thresholds [11]. Both percentages of agreement and weighted Cohen's kappa increased at both femur (weighted Cohen's $k = 0.87$; percentage agreement: 86.7%) and spine (weighted Cohen's $k = 0.87$; percentage agreement: 83.6%), further reinforcing the diagnostic agreement between DXA and REMS technologies. These results are in line with previous evidence showing good diagnostic agreement between DXA and REMS measurements at both reference anatomical sites [11, 12], further supporting the use of REMS technology in osteoporosis management as a more accessible alternative to standard DXA [25, 26]. Additional insight may be obtained from analysis of the remaining discordant cases, corresponding to 17 of 128 patients at the femoral site (13.2%), and 21 of 128 patients (16.4%) at the spinal site. At the femur, 14 of the 17 discordant cases (82.4%) were reclassified into higher risk categories by REMS compared with DXA. Among these, for example, 3 patients (21.4%) were affected by type 2 diabetes mellitus (T2DM) and showed high FS values, with a median of 45.6 (Q1–Q3: 41.0–61.4), indicating impaired bone quality. Consistently with their clinical condition, these patients were reclassified by REMS into higher-risk categories than DXA. This finding is clinically relevant, as patients with T2DM have been reported to show a 1.9-fold higher fracture risk compared with non-diabetic individuals, despite often showing normal or even increased BMD [27–29]. This condition, known as the diabetic bone paradox, suggests that bone quality, rather than bone quantity alone, plays a crucial role in skeletal fragility in diabetic patients [30]. In this context, REMS-derived parameters may provide additional information on bone quality that is not fully captured by DXA [31]. A similar pattern was observed in another 5 of the 14 upward-reclassified discordant cases (35.7%), which showed high FS values (median 42.5, Q1–Q3: 42.3–55.5), consistent with markedly impaired bone quality. These findings further suggest that bone quality may play an important role in fracture risk classification and may not be adequately captured by DXA-derived BMD alone. Among the remaining discordant cases ($n = 9$), most were reclassified into adjacent risk categories (5/9), while only 4 cases showed non-adjacent discordance.

Regarding the spine, 17 of 21 discordant cases (81%) were reclassified into higher risk categories by REMS compared with DXA. Among these, 8 patients (8/17, 47.1%) had a history of previous vertebral fracture(s), a condition that may be associated with vertebral deformities and local structural changes potentially affecting lumbar DXA measurements [32]. Of the remaining 13 discordant cases, 9 were reclassified by REMS into adjacent risk categories.

Overall, these findings suggest that discrepancies between DXA- and REMS-based classifications were generally limited, and may partly reflect observations that artefacts affecting densitometry results usually lead to overestimation of BMD for DXA [33].

After assessing agreement between DXA-based and REMS-substituted DVO categories, the distributions of Fragility Score values and REMS 5-year fracture risk classes across REMS-substituted DVO categories were explored. A progressive increase in Fragility Score values across increasing DVO 2023 risk thresholds was found. This trend was observed at both femoral and spinal sites, suggesting internal consistency between the REMS-based DVO clinical-risk framework and a REMS-derived parameter reflecting skeletal fragility. Fragility Score is designed to provide information on bone quality and microarchitectural deterioration that is not fully captured by BMD alone [10], further supporting the hypothesis that REMS may provide complementary information beyond densitometric classification. Similarly, the distribution of REMS 5-year fracture risk classes (R1 to R7) showed a progressive shift toward higher-risk categories with increasing REMS-based DVO 2023 thresholds, and this pattern was evident for both hip fracture risk (calculated at the femoral site) and major osteoporotic fracture risk (calculated at the spinal site). These findings further support the internal coherence between REMS-derived fracture risk stratification and DVO-based clinical risk categories. However, the two predictive tools differ in their time horizon: while DVO 2023 estimates a 3-year risk of vertebral and proximal femoral fractures, REMS fracture risk stratification provides 5-year probability ranges for major osteoporotic or hip fractures.

From a clinical point of view, these findings may be relevant for the implementation of individualized osteoporosis risk assessment. The DVO 2023 update emphasizes risk-adapted treatment decisions, spanning from early intervention in selected patients within the 3% to < 5% risk corridor, to recommendation of specific pharmacological therapy in patients classified in the 5% to < 10% corridor, to prioritization of osteoanabolic treatment in patients at very high risk ($\geq 10\%$) [2]. In this context, REMS technology could potentially support fracture risk stratification by providing both densitometric and quality information. This may be particularly useful in scenarios where clinical applicability is reduced by DXA limitations. In addition, this internal coherence may potentially support the use of REMS predictive parameters in fracture risk stratification when risk factor information is missing or not completely available.

This study has some limitations. First, its retrospective, single-center design. Second, only clinical risk factors systematically available in the medical records and compatible with the web-based DVO calculator were included; however, the same clinical risk factors were always applied to both DXA-based and REMS-substituted calculations, preserving the internal validity of the comparison between the two densitometric approaches. Finally, this study did not include longitudinal follow-up that could directly evaluate the predictive performance of REMS-substituted DVO estimates for incident fractures versus DXA-based DVO estimates.

Conclusion

The DVO 2023 guideline introduced an updated 3-year fracture-risk framework integrating DXA-derived T-scores with anthropometric, demographic and clinical risk factors [5]. This retrospective observational study demonstrated for the first time that DXA-based DVO categories showed high agreement with

REMS-substituted DVO categories at both femur (81.2%, weighted Cohen's $k = 0.84$) and spine (80.5%, weighted Cohen's $k = 0.85$), which further increased after applying the ± 0.3 tolerance at T-score thresholds (percentage agreement: 86.7% and 83.6%; weighted Cohen's $k = 0.87$ and 0.87 at femur and spine, respectively). Furthermore, FS values and REMS 5-year fracture risk classes increased across higher REMS-substituted DVO categories, supporting the clinical coherence of REMS-derived skeletal fragility and fracture risk prediction parameters. Overall, these findings support the potential use of REMS as an alternative, radiation-free approach for fracture risk stratification within DVO-based clinical pathways.

Declarations

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Competing interests

The authors have no relevant financial or non-financial interests to disclose.

Ethics approval

This study was approved by the Ethics Review Board of the Landesärztekammer Hesser, Germany and was conducted in accordance with the ethical standards of the 1964 Declaration of Helsinki and its subsequent amendments.

Consent to participate

Informed consent for participation and publication was obtained from all participants included in the study.

Consent to publish

Not applicable; this manuscript does not contain any individual person's identifiable data, images or other personal or clinical details.

Data availability

All relevant data will be made available upon reasonable request and under a dedicated agreement with the corresponding author.

Author contributions

All three authors contributed to the study conception, design and recruiting patients. Prof. Dr. Andreas Kurth has performed all the REMS measurements, has done the data and statistical analysis and written

the 1. draft of the manuscript. Dr. Julius Baron and Dr. Joachim Baron have recruited patients for the screening of osteoporotic risk factors and helped to write the drafts. All authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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Figures

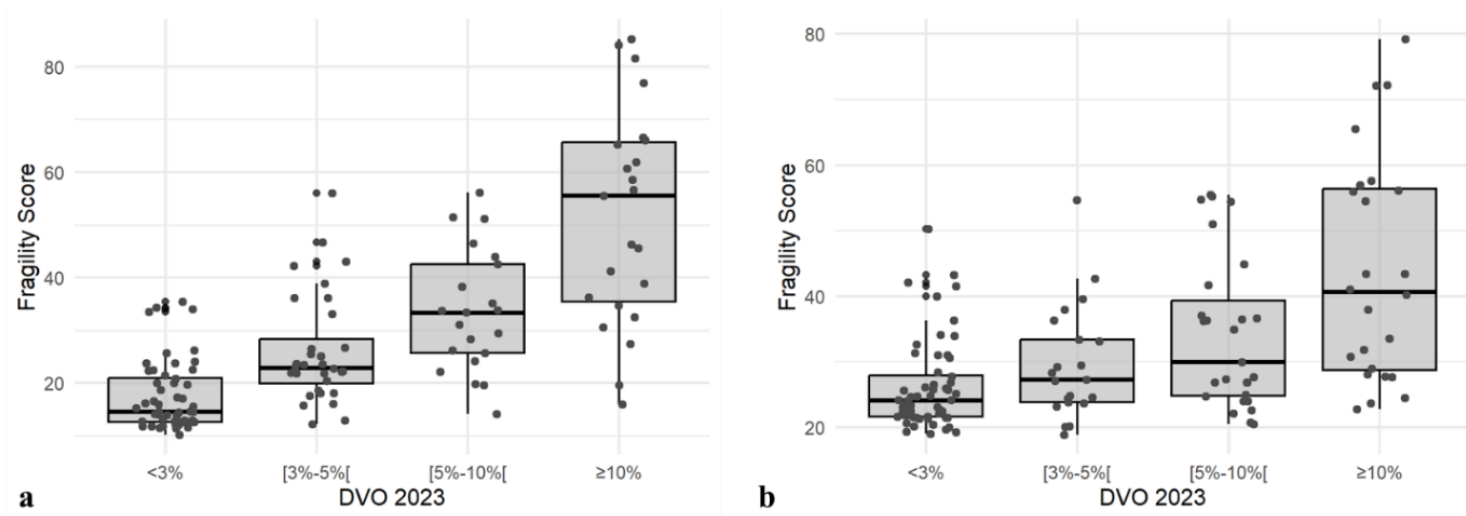


Figure 1

Boxplot distribution of Fracture Risk Score by DVO 2023 threshold categories (<3%, 3% to <5%, 5% to <10%, ≥10%) for femoral (a) and spine (b) scans