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Original Article

Comparative Evaluation of Osteoporosis Clinical Risk Assessment Tools in Postmenopausal Women Aged 50-64

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Abstract

Objectives: To assess the performance of five osteoporosis clinical risk assessment tools (SCORE, ORAI, ABONE, OST and OSIRIS), in a subgroup of young postmenopausal women aged 50-64, who underwent DXA screening. **Methods**: The above-mentioned osteoporosis risk assessment tools were calculated for 258 young postmenopausal women (aged 50-64) who had a DXA scan, in Crete/Greece. **Results**: Patients with a T-score ≤ -2.5 or a T-score ≤ -2.0 had a statistically significant higher value of SCORE, ORAI and ABONE and a lower value of OST, OSIRIS, and OSIRIS Adjusted Score, compared to the patients with T-score > -2.5 and T-score > -2.0, respectively. ORAI (T-score≤ -2.0) and OST (T-score≤ -2.5) demonstrated the highest sum of sensitivity and specificity. CHAID analysis further confirmed the relative significance of the OST tool in the osteoporosis group (T-score≤ -2.5 vs. T-score > -2.5), for a cut-off of 2.8. In the other group (T-score ≤ -2.0 vs T-score > -2.0) the ORAI score showed a significantly important relationship for a cut-off of 8. **Conclusion**: OST, despite its performance limitations, correlates best with the DXA measurements of young (50-64), postmenopausal osteoporotic women, a fact which may suggest its' potential role as a screening tool in this specific age group.

Keywords: DXA, Osteoporosis, Osteoporosis Clinical Risk Assessment Tools, Osteoporosis Screening, Postmenopausal Women

Introduction

Osteoporosis has been defined as a systematic skeletal disorder, characterized by reduced bone quantity and quality, which result to compromised bone strength, thus predisposing to an increased risk of fracture[1]. Half of all postmenopausal women will suffer an osteoporotic fracture during their lifetime[2], which is of particular importance since osteoporotic fractures are commonly associated with chronic pain and disability, loss of independence, reduced quality of life and increased mortality[3].

The parameter which is most commonly used to determine bone strength is bone mineral density (BMD), defined as the concentration of the mineral elements of bone, per unit volume (vBMD). The World Health Organization (WHO) definition on osteoporosis is based on Dual-energy X-Ray Absorptiometry (DXA), which is a two-dimensional technique, so BMD is defined by DXA as the concentration of the mineral elements of bone, per unit area (aBMD)[4]. Decrease in bone density, both perimenopausal and in the first years after menopause, is known to be significant (half of the lifetime bone loss is lost during the first 10 years after menopause)[5], especially in cases of early menopause of any etiology[6].

Most published guidelines recommend DXA screening for women 65 years and older. Screening for younger postmenopausal women aged 50 to 64 years is based on the presence of risk factors[7]. It is important to identify the at-risk women of this age group who may benefit from

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Table 1. Variables utilized for the calculation of the clinical risk assessment tools and calculation algorithm.

Clinical risk assessment tool	Variables	Calculation Algorithm
SCORE	• Rheumatoid arthritis (RA) (YES=+4/NO=0) • Osteoporotic fracture history (OFH) (spine, wrist, ribs, hip) (+4 for every known fracture / maximum +12) • Estrogen (ES) (Prior use=0 / No use=1) • Age^{I} (= 3 * Age^{II} / 10) • Weight^{I} (= Weight^{II}/10)	SCORE = RA+OFH+ES+Age^{I}-Weight^{I}
ORAI	• Estrogen (ES) (Prior use=0 / No use=2) • Age^{I} o If Age^{II} ≥75 = 15 o If Age^{II} ≥65 and <75 = 9 o If Age^{II} ≥55 and <65 = 5 o Else Age^{I} = 0 • Weight^{I} o If Weight^{II} <60 = 9 o If Weight^{II} <70 and ≥60 = 3 o Else Weight^{I} = 0	ORAI = Age^{I}+Weight^{I}+ES
ABONE	• Age^{I} o If Age^{II} > 65 = 1 o Else Age^{I} = 0 • Weight! o If Weight^{II} <63.5 = 1 o Else Weight^{I} = 0 • Estrogen (ES) (Prior use=0 / No use=1)	ABONE=Age^{I}+Weight^{I}+ES
OST	• Age^{I} = Age^{II} • Weight^{I} = Weight^{II}	OST=0.2*(Weight^{I}-Age!)
OSIRIS	• Age^{I} = first digit of (-0.2 * Age^{II}) • Weight^{I} = first digit of (0.2 * Weight^{II}) • Estrogen (ES) (Prior use=+2 / No use=0) • Low impact fracture history (LIFH) (Yes=-2 / No=0)	OSIRIS=Age^{I}+Weight^{I}+ES+LIFH
OSIRIS Adjusted Score	• Age^{I} = rounded to the nearest integer (-0.2 * Age^{II}) • Weight^{I} = rounded to the nearest integer (0.2 * Weight^{II}) • Estrogen (ES) (Prior use=+2 / No use=0) • Low impact fracture history (LIFH) (Yes=-2 / No=0)	OSIRIS Adjusted score = Age^{I}+Weight^{I}+ES+LIFH
Age$^{(I)}$ = calculated age. Weight$^{(I)}$ = calculated weight. Age$^{(II)}$ = age in years. Weight$^{(II)}$ = weight in kg.		

osteoporosis screening and depending on the results, early initiation of treatment aiming to prevent fractures[8].

The aim of our study was to assess the performance of five osteoporosis clinical risk assessment tools (Simple Calculated Osteoporosis Risk Estimation (SCORE)[9], Osteoporosis Risk Assessment Instrument (ORAI)[10], Age Bulk One or Never Estrogen (ABONE)[11], Osteoporosis Self-Assessment Tool (OST)[12] and Osteoporosis Index of Risk (OSIRIS)[13]), in correlating with the DXA measurements of young postmenopausal women aged 50-64. Depending on the results, our study aimed to identify the best performing clinical risk assessment model, to be further evaluated as a screening tool, to identify the subgroup of women that would benefit from DXA screening.

Materials and Methods

This was a cross-sectional study, which included young postmenopausal women (age in years ≥50 and <65), who presented to a diagnostic imaging unit in Crete/Greece, with a referral for a DXA scan, according to the guidelines for the diagnosis and treatment of osteoporosis in Greece[14], from March 2023 to December 2023.

Patients already under treatment for osteoporosis, with known co-morbidities (including hyperparathyroidism, hyperthyroidism, renal disease) or use of medications (corticosteroids for more than 3 months, heparin) that might have caused bone loss were excluded from the study. Collected data included the date of birth, height and weight,

history of osteoporotic fracture, history of rheumatoid arthritis and history of estrogen use.

According to the guidelines of the International Society for Clinical Densitometry (ISCD), measurement of bone density with DXA included the assessment of BMD in three anatomical regions (Lumbar Spine, Total Hip and Femoral Neck)[15]. The lowest T-score value was then used for the final diagnosis[16]. A T-score ≥-1.0 indicated normal bone density, a T-score <-1.0 and >-2.5 diagnosed osteopenia (low bone mass) and a T-score ≤-2.5 diagnosed osteoporosis.

We calculated the values of five osteoporosis clinical risk assessment tools (SCORE, ORAI, ABONE, OST, OSIRIS) for all the patients of our study group, plus an OSIRIS Adjusted score, which was calculated by rounding the source values to the nearest integer. The variables and algorithms which were utilized for the calculation of each clinical risk assessment tool are listed in Table 1.

We divided the participants of our study into three groups: (1) normal (T-score≥1) and osteopenic women with a T-score>-2.0, (2) osteoporotic women (T-score ≤ -2.5) and (3) osteopenic women with a T-score ≤ -2.0. Selection of the last group was justified by the intrinsic design and the validation process of some of the clinical risk assessment tools (T-scores of both -2.5 and -2.0 are used as thresholds in the published literature referring to the performance of the scores)[17] and by the fact that a proportion of the women in that group might benefit from treatment, depending on their FRAX score calculation[18].

Statistical Analysis

Data were expressed as mean ± standard deviation (SD) for continuous variables and as percentages for categorical variables. The Kolmogorov-Smirnov test was utilized for normality analysis of the continuous variables.

Independent samples t-test was used for the comparison of clinical risk assessment tools between groups (T-score ≤-2.5 vs T-score >-2.5) and (T-score ≤-2 vs T-score >-2). A receiver operating curve (ROC) analysis was conducted to examine their prognostic ability to discriminate between groups (T-score ≤-2.5 vs T-score >-2.5) and (T-score ≤-2 vs T-score >-2), by calculating the respective areas under the curve (AUC) with 95%CI. Cut-off points which maximize the sum of sensitivity (sensitivity) and specificity (specificity), were estimated. Furthermore, PPV and NPV of different cut-off points were also estimated.

Chi-square Automatic Interaction Detector (CHAID) analysis was used to build a predictive model, or tree to determine how the clinical risk assessment tools best merge to explain the outcome variables (T-score ≤-2.5 vs T-score >-2.5) and (T-score ≤-2 vs T-score >-2). All the tests were two-sided, and statistical significance was set at p < 0,05.

All analyses were carried out using the statistical package SPSS V21.0 (IBM Corporation, Somers, NY, USA).

Table 2. Osteoporosis clinical risk assessment tools calculations.

SCORE; Mean±SD (min-max)	8.00±3.21 (-4.0 / 15.0)
ORAI; Mean±SD (min-max)	8.80±4.10 (1.0 / 20.0)
ABONE; Mean±SD (min-max)	1.29±0.46 (0.0 / 2.0)
OST; Mean±SD (min-max)	2.51±2.86 (-3.6 / 12.5)
OSIRIS; Mean±SD (min-max)	2.54±2.86 (-4.0 / 12.0)
OSIRIS Adjusted Score; Mean±SD (min-max)	2.55±2.91 (-4.0 / 13.0)

Results

Two hundred and fifty-eight women (258) with an age ≥50 years and <65 years participated in the study. The mean age of the patients was 57.61 years ±3.78(min 50 – max 64.76), the mean weight was 70.19 kg ±14.20 (min 39.5 – max 124.0), the mean Body Mass Index (BMI) was 27.88 kg/cm^2 ±5.61 (min 17,32 – max 49,67) and the mean height was 158.78 cm ±5.91 (min 142.0 – max 176.0).

One hundred and forty-eight (148) of the participants had osteopenia (57.4%), fifty-two (52) had osteoporosis (20.2%) and fifty-eight (58) were normal (22.4%). In one hundred and forty-four (144) of them (55.8%) the diagnostic (lowest) T-score value was measured at the lumbar spine, in seventy-three (73) (28.3%) at the femoral neck and in forty-one (41) (15.9%) at the total hip. Of the osteoporotic group of patients, in thirty-nine (39) (75%) the diagnostic (lowest) T-score value was measured at the lumbar spine, in six (6) (11.5%) at the femoral neck and in seven (7) (13.5%) at the total hip.

Referring to medical history, six (6) patients had a history of Rheumatoid Arthritis, one (1) patient had a history of a fragility fracture, and two (2) patients had a history of estrogen administration post-menopause.

Mean values, standard deviations, and lower/upper limits of the osteoporosis clinical risk assessment tools which we evaluated are summarized in Table 2.

Statistical analysis proved that:

Patients with a T-score ≤-2.5 or with a T-score ≤-2.0, demonstrated statistically significant higher values of SCORE (p<0.0005), ORAI (p<0.0005) and ABONE (p<0.0005), and statistically significant lower values of OST (p<0.0005), OSIRIS (p<0.0005) and OSIRIS Adjusted Score (p<0.0005), compared with those with a T-score >-2.5 or with a T-score >-2.0, respectively. Cohen's thresholds demonstrated a moderate effect of the calculated scores.

Comparison results are demonstrated in Table 3.

ROC analysis based on a T-score value of ≤ -2.0 or > -2.0, proved that the tool with the highest value of the Area Under the Curve (AUC) was OSIRIS (AUC: 0.680), followed by the OST (AUC: 0.673) and in the third place, were the SCORE

Table 3. Comparison of clinical scores between groups, based on the T-score.

	T-score >-2.5 (n=205)*	T-score ≤-2.5 (n=53)*	Effect Size (Cohen's)**	p-value
SCORE	7.60±3.31	9.51±2.26	0.78	<0.0005
ORAI Score	8.35±3.91	10.55±4.31	0.54	<0.0005
ABONE Score	1.23±0.44	1.51±0.50	0.64	<0,0005
OST Score	2.90±2.94	1.02±1.92	0.78	<0.0005
OSIRIS Score	2.94±2.93	1.00±1.95	0.78	<0,0005
OSIRIS Adjusted Score	2.94±3.01	1.08±1.91	0.74	<0.0005
	T-score >-2.0 (n=169)	T-score ≤-2.0 (n=89)	Effect Size (Cohen's)**	p-value
SCORE	7.39±3.36	9.15±2.55	0.59	<0,0005
ORAI Score	7.93±3.62	10.45±4.42	0.62	<0.0005
ABONE Score	1.22±0.43	1.43±0.50	0.45	<0,0005
OST Score	3.11±2.98	1.38±2.21	0.66	<0.0005
OSIRIS Score	3.17±2.97	1.35±2.21	0.69	<0,0005
OSIRIS Adjusted Score	3.13±3.07	1.46±2.23	0.62	<0.0005

** All values are presented as mean±SD. ** Cohen's thresholds (>0.8 large; 0.5 to 0.8 moderate, and <0.5 small).*

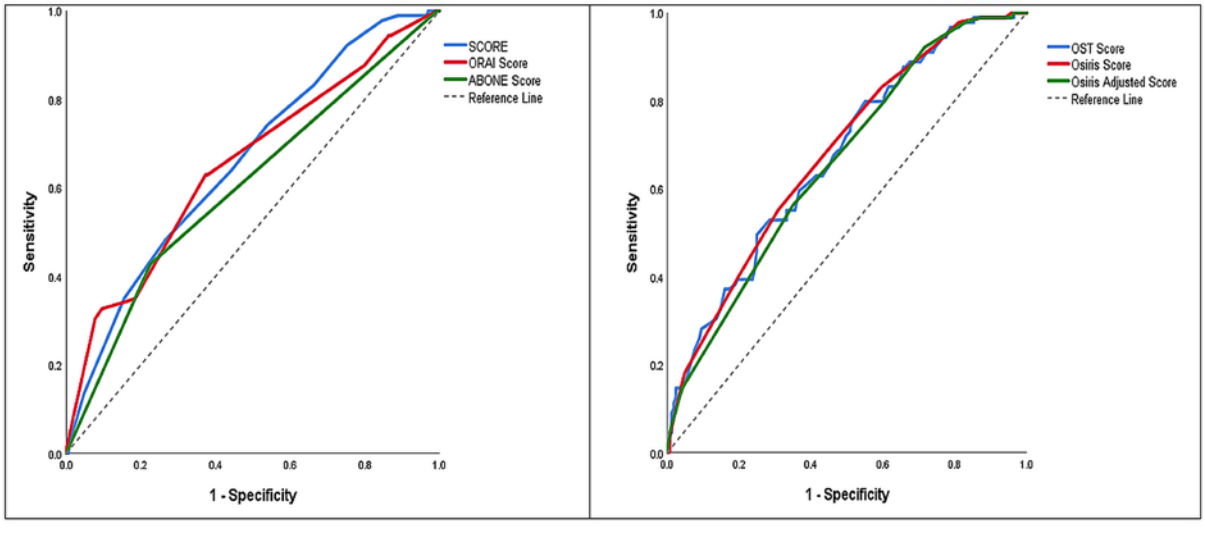

Figure 1. ROC analysis of clinical scores for a T-score cut-off of (-2).

and the OSIRIS Adjusted Score (AUC: 0.658). The highest sensitivity was demonstrated by SCORE (64%), followed by ORAI (63%) and OSIRIS Adjusted Score (56%). ABONE (78%), OST (75%) and OSIRIS (70%), demonstrated the highest specificity values. The best Positive Predictive Value (PPV) was demonstrated by the OST Score (51%), followed by ABONE (50%) and OSIRIS (48%). The tool with the highest Negative Predictive Value (NPV) was ORAI (76%), followed by SCORE (75%), OSIRIS (75%) and OSIRIS Adjusted Score (75%) (Table 4, Figure 1).

ROC analysis of the clinical risk assessment tools based on a T-score value of ≤ -2.5 or > -2.5, proved that the tool with the highest value of the Area Under the Curve (AUC) was OSIRIS (AUC: 0.696), followed by the OST (AUC: 0.690) and the OSIRIS Adjusted Score (AUC: 0.680). The highest sensitivity was demonstrated by OST (89%), followed by SCORE (84%) and OSIRIS Adjusted Score (79%). ABONE (76%) and ORAI (60%), demonstrated the highest specificity values. The best Positive Predictive Value (PPV) was demonstrated by ABONE (35%) and ORAI (31%). The tool with the highest Negative

Table 4. ROC analysis of clinical risk assessment tools for T-score≤-2.0 and T-score>-2.0.

	AUC	SE	95% CI		p-value	Cut-off point	Sensitivity	Specificity	PPV	NPV
SCORE*	**0.658**	0.035	0.59	0.73	**<0.0005**	8.5	64%	56%	43%	75%
ORAI Score*	**0.652**	0.037	0.58	0.72	**<0.005**	9.0	63%	63%	47%	76%
ABONE Score*	**0.603**	0.038	0.53	0.68	**0.007**	1.5	43%	78%	50%	72%
OST Score†	**0.673**	0.034	0.61	0.74	**<0.005**	1.05	50%	75%	51%	74%
Osiris Score†	**0.680**	0.034	0.61	0.75	**<0.005**	1.50	55%	70%	48%	75%
Osiris Adjusted Score†	**0.658**	0.035	0.59	0.73	**<0.005**	1.50	56%	65%	46%	75%

*AUC: Area Under the Curve, SE: standard error, CI: confidence interval. * Larger values of the test result variable indicate stronger evidence for T-score≤-2.0. † Smaller values of the test result variable indicate stronger evidence for T-score≤-2.0.*

Table 5. ROC analysis of clinical risk assessment tools for T-score≤-2.5 and T-score>-2.5.

	AUC	SE	95% CI		p-value	Cut-off point	Sensitivity	Specificity	PPV	NPV
SCORE*	**0.672**	0.039	0.60	0.75	**<0.0005**	7.5	84%	44%	27%	90%
ORAI Score*	**0.643**	0.044	0.56	0.73	**0.001**	9.0	70%	60%	31%	88%
ABONE Score*	**0.636**	0.045	0.55	0.72	**0.002**	1.5	51%	76%	35%	86%
OST Score†	**0.690**	0.038	0.62	0.76	**<0.005**	2.95	89%	45%	30%	94%
Osiris Score†	**0.696**	0.037	0.62	0.77	**<0.005**	2.50	79%	51%	30%	90%
Osiris Adjusted Score†	**0.680**	0.038	0.61	0.75	**<0.005**	2.50	77%	50%	28%	89%

*AUC: Area Under the Curve. SE: Standard Error. CI: Confidence Interval. * Larger values of the test result variable indicate stronger evidence for T-score≤-2.5. † Smaller values of the test result variable indicate stronger evidence for T-score≤-2 .5.*

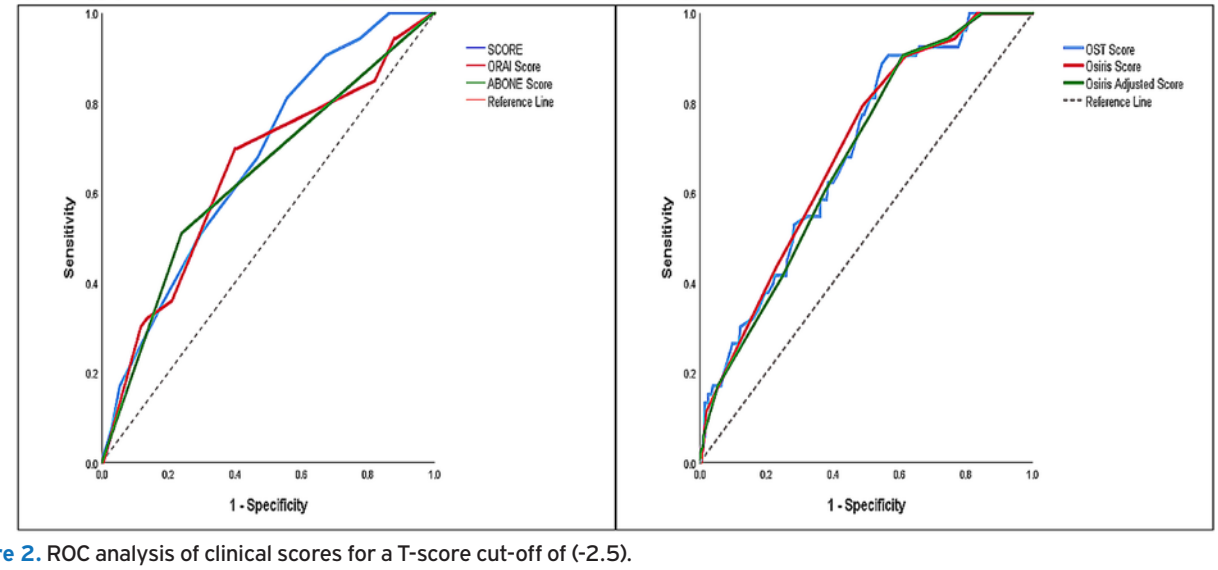

Figure 2. ROC analysis of clinical scores for a T-score cut-off of (-2.5).

Predictive Value (NPV) was OST (94%), followed by SCORE (90%) and OSIRIS (90%) (Table 5, Figure 2).

CHAID Analysis (quantitative variables)

(a) T-score ≤-2.0 vs. T-score >-2.0 (Figure 3): The ORAI clinical risk assessment tool was the only statistically significant discriminator. The highest percentage for a T-score ≤-2.0 appeared in the subgroup with ORAI >8 (47.1%), which was 12,6% higher than the corresponding percentage of the total sample (34.5%).

(b) T-score ≤-2.5 vs. T-score >-2.5 (Figure 4): The OST clinical risk assessment tool was the only statistically significant discriminator. The highest percentage for a T-score ≤-2.5 appeared in the subgroup with OST < 2.8 (29.2%), which was 10% higher than the corresponding percentage of the total sample (20.5%).

Results summary

- ROC analysis failed to confirm clear superiority of any of the analyzed osteoporosis clinical risk assessment tools. Their performance was average (AUC range of 0.600 to 0.680 for a T-score ≤ -2.0 and AUC range of 0.636 to 0.696 for a T-score ≤ -2.5).
- ORAI (T-score≤ -2.0) and OST (T-score≤ -2.5) demonstrated the highest sum of sensitivity and specificity.
- CHAID analysis further confirmed the relative significance of the OST tool in the osteoporosis group (T-score≤-2.5 vs. T-score >-2.5), when OST was smaller than a cut-off of 2.8. In the other group (T-score ≤-2.0 vs T-score >-2.0), it was the ORAI score which showed a significantly important relationship with the diagnostic category cut-off of 8.

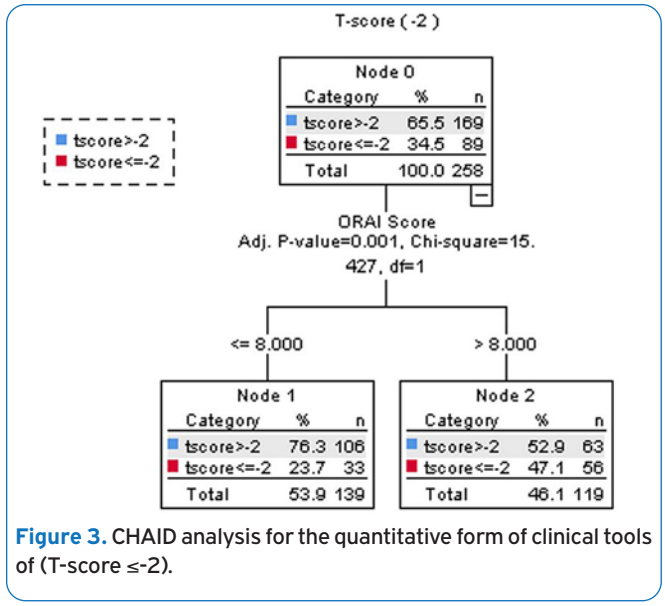

Figure 3. CHAID analysis for the quantitative form of clinical tools of (T-score ≤-2).

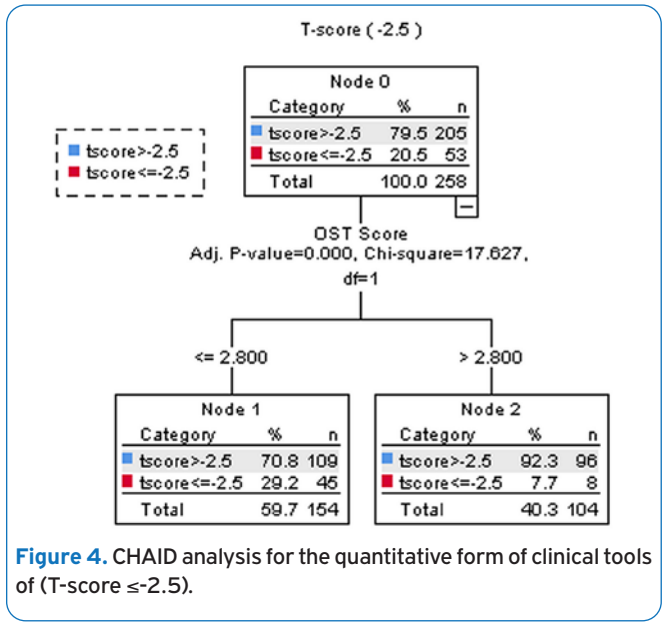

Figure 4. CHAID analysis for the quantitative form of clinical tools of (T-score ≤-2.5).

Discussion

DXA osteoporosis screening in the young postmenopausal women (<65y) is mainly based on the presence of risk factors, the exact definition and identification of which, may be quite complicated and ambiguous, since there is no general agreement among the scientific groups / societies 15,18–21. On the other hand, the presence of at least one of the risk factors in a significant percentage of the population, makes the selection process ineffective[22].

The main advantage of the osteoporosis clinical risk assessment tools, the performance of which we evaluated in a Greek – Mediterranean population, is their simplicity. They have been extensively tested and validated and it has been proposed that they may be used as screening tools to guide further screening with DXA, thus minimizing the number of unnecessary examinations[10,23–29]. Combining the above-mentioned clinical scores with the Fracture Risk Assessment Tool (FRAX) or with any of the identified risk factors (or combinations of risk factors), in an effort to increase their screening performance, has been proposed[25].

Our study suggested that the OST score, correlated best with the DXA measurements in this patient subgroup (postmenopausal women aged 50-64), especially in osteoporotic patients (as defined by WHO: DXA T-score≤-2.5). OST is a very simple tool/model, based on basic (administrative) data (age and weight), which may be easily collected for any patient. As a result, it may easily be further evaluated as a predictor in an osteoporosis screening setting, to triage selective DXA screening. This agrees with published literature[24,25,30].

The main problem with the evaluation of the performance of the clinical risk assessment tools is the heterogeneity of the design of the published studies, which is due to (a) different population / age groups studied, (b) due to different thresholds (cut-off) values and (c) due to (slightly) different calculation formulas. As was suggested in a meta-analysis / systematic review which evaluated various clinical risk assessment tools[17], sensitivity is expected to be lower in younger patients (and specificity, consequently higher), compared to older patients. On the other hand, increasing the sensitivity aiming to detect more patients with clinically significant osteopenia or osteoporosis, would result to the consequent lowering of specificity, thus yielding many false positive results. What is very important, in any case, is the definition of the exact cut-off values, which may be age or population dependent[17].

The main limitation of this study is the small number of patients. However, there are very limited published data evaluating the use of clinical scores in this age sub-category and even more limited related to a Greek Mediterranean population. The only published study that we are aware of evaluates the clinical scores in a Greek population from the North - Eastern part of Greece (Eastern-Macedonia, Thrace), consisting of postmenopausal women, however without age limits[31].

In conclusion, according to our results, OST, either alone or combined with other clinical risk assessment tools, despite its performance limitations, offers an attractive clinical tool, which may be further evaluated as a predictor, to identify a subgroup of the young (50-64), postmenopausal osteoporotic women (DXA T-score ≤ 2.5) who would benefit from osteoporosis screening with DXA, thus reducing the number of patients undergoing unnecessary DXA scans. The other, still simple, however more complex than OST, osteoporosis clinical risk assessment tools (SCORE, ORAI, ABONE, OSIRIS), did not offer any advantages over the use of OST, as our analysis proved, with the exception of ORAI, in the group of women with osteopenia (T-score≤ -2.0).

Ethics approval

According to Greek legislation, the study was ethically approved by the Scientific Director of the laboratory (primary healthcare unit).

Consent to participate

Written informed consent was acquired from the participants.

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