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Original Article

Evaluation of Different Screening Tools for Predicting Femoral Neck Osteoporosis in Rural South Indian Postmenopausal Women

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Abstract

The measurement of bone mineral density by dual-energy X-ray absorptiometry scan is the "gold standard" for the diagnosis of osteoporosis, which has limited availability in many parts of India. This study was done to assess the diagnostic performance of 6 internationally validated tools (Simple Calculated Osteoporosis Risk Estimation [SCORE], age, bulk, one or never estrogen [ABONE], Osteoporosis Risk Assessment Instrument [ORAI] and Osteoporosis Self-Assessment Tool for Asians [OSTA], Fracture Risk Assessment Tool [FRAX®], and calcaneal quantitative ultrasound [QUS]) for the diagnosis of osteoporosis at the femoral neck (FN). This was a cross-sectional study conducted in 2108 ambulatory South Indian rural postmenopausal women who were assessed with SCORE, ABONE, ORAI, OSTA, and FRAX® tools. QUS was performed in 850 subjects. Bone mineral density was estimated by dual-energy X-ray absorptiometry scan at the FN, and sensitivity and specificity were calculated for all tools for predicting FN osteoporosis. The receiver operating characteristic curve was constructed for each tool and the area under the curve (AUC) was calculated. FN osteoporosis was seen in 27%. The sensitivities of SCORE, ABONE, OSTA, ORAI, FRAX®, and QUS were 91.3%, 91.0%, 88.5%, 81.0%, 72.7%, and 81.9%, and the specificities were 36.0%, 33.5%, 41.7%, 52.0%, 60.5%, and 50.3%, respectively, for the FN osteoporosis. When the receiver operating characteristics were constructed, the AUC was good only for SCORE (0.806), and the performance of the rest was under fair category (0.713–0.766). In our large cohort of rural postmenopausal women, the SCORE screening tool was found to be useful with good sensitivity and good AUC for predicting FN osteoporosis. Thus, this tool may be used in resource-limited countries to screen the population at risk and to enable treating physicians to make appropriate management decisions.

Key Words: Osteoporosis; postmenopausal women; risk assessment tools SCORE.

Introduction

The number of Indian women diagnosed with osteoporosis is on the rise, paralleling the increase in their life expectancy *(1)*. Postmenopausal osteoporosis is the most common metabolic bone disease and occurs following the cessation of the ovarian function, leading to a dramatic decrease in female sex hormones. In addition, the poor dietary intake of calcium and vitamin D deficiency has been widely reported in the Indian subcontinent, which further contributes to adverse bone health *(2)*.

Osteoporosis is characterized by a reduction in bone density and poor bone quality, leading to an increased fragility and the development of fractures. Osteoporosis is defined by the World Health Organization *(3)* as a value of bone mineral density (BMD), 2.5 standard

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deviations (SDs) below the young female adult mean (a *T*-score of ≤−2.5). The number of postmenopausal women above 50 yr of age is about 100 million, and more than two-thirds of them reside in the rural area. About 40%–50% of postmenopausal women have osteoporosis. The gold standard tool for the diagnosis of osteoporosis is the dual-energy X-ray absorptiometry (DXA) scan. However, the restricted availability of DXA *(4)*, coupled with a lack of portability and poor affordability, make it inaccessible to the majority of older women in rural and suburban areas, which bear the brunt of this debilitating condition. Osteoporosis is a clinically silent disease unless complicated by fractures *(5)*, and this calls for active surveillance to establish the diagnosis early and with certainty. The crude incidence rate of osteoporotic fractures at the hip was approximately estimated to be 159/100,000 women per year in a study done by Dhanwal et al in northern India *(6)*.

Osteoporotic fractures pose a tremendous burden on the community, in terms of loss of productivity, increased morbidity *(7)*, prolonged hospital stay, and the huge costs involved in the treatment and rehabilitation of those affected. A recent study from south India has shown that about one-fifth of those who had sustained a hip fracture died by the end of 1 yr *(8)*.

It is therefore imperative to employ reasonably priced alternatives that will cater to the meager resources of rural-dwelling women. The use of quantitative ultrasound (QUS) and multiple risk scoring systems may enable a cost-effective mass screening for osteoporosis in the community.

There has been some interest in the use of clinical risk assessment tools to screen for osteoporosis before a DXA scan *(9)*. These tools serve to analyze the various risk factors for individual patients and thereby assess as to whether the presence of these risk factors warrant further evaluation with a DXA scan. A total of 48 such risk assessment tools have been identified, of which 20 have been externally validated. Eight of these tools were designed to identify subjects at risk of low BMD and 12 were developed to predict fractures *(10)*. There was a significant trade-off seen between sensitivity and specificity for most of the screening tools in previously published literature.

However, there is a paucity of information with regard to the application of these tools in an Indian context. If these tools are found to be appropriate with good sensitivity and acceptable specificity, they can be utilized as effective screening tools. So, we attempted to study the performance characteristics of 6 internationally validated screening tools in predicting osteoporosis at the femoral neck (FN) in rural postmenopausal Indian women.

Methodology

This was a cross sectional study done from October 1, 2014, to March 31, 2016. The study was approved by the institutional review board.

Study Subjects

All ambulatory rural postmenopausal women aged 50 yr and above were recruited from the Vellore district of southern India. Women with a prior diagnosis of osteoporosis, malignancy, stroke, or other conditions leading to immobilization, chronic kidney disease, and chronic liver disease were excluded. Those women on treatment with bisphosphonates and anabolic agents were also excluded.

Sample Size

The number of rural postmenopausal woman in the study area was 180,688. The sample size of 2149 was calculated, keeping a power (1 − β) of 80% to produce a statistically significant (α level) 5% based on the sensitivity of Simple Calculated Osteoporosis Risk Estimation (SCORE) that has been published in a previous study *(9)*.

Data Collection

DXA Scan

After obtaining informed consent from the subjects, the estimation of BMD was done at the FN using the DXA scanner (Hologic-QDR 4500-W Discovery-A; Hologic Inc, Bedford, MA, USA). The National Health and Nutrition Examination Survey (NHANES) III Caucasian normative data were used as the reference database in this Hologic machine *(11)*. The subjects were classified as osteoporosis, osteopenia, and normal, depending on the World Health Organization *T*-scores (at the FN) of ≤−2.5, −2.5 to −1.0, and normal ≥−1, respectively. The precision of the DXA scanner for this measurement was about 2%.

Tools

The various screening tools used in this study were

1. SCORE *(12,13)*
2. Age, Bulk, One Or Never Estrogen (ABONE)*(14)*
3. Osteoporosis Self-Assessment Tool for Asians (OSTA) *(15)*
4. Osteoporosis Risk Assessment Instrument (ORAI) *(16)*
5. Fracture Risk Assessment Tool (FRAX®) India (without BMD) *(12)*
6. QUS: BMD estimation with quantitative heel ultrasound (QUS) has been shown to be a predictor for osteoporosis in various studies *(17,18)*. In our study, we used the Japanese-made CM-200 ultrasound bone densitometer, which has been utilized previously *(19)*. The CM-200 measures the speed of sound transmitted through the calcaneum. Sound waves generated from 1 transducer passed through the subject's right heel and were received by the other transducer. The footpad was individually adjusted according to the size of the foot *(19)*. QUS was performed in 850 subjects and had a CV of 3%.

SCORE was developed in a cohort of 1102 postmenopausal women and used the parameters of race, the

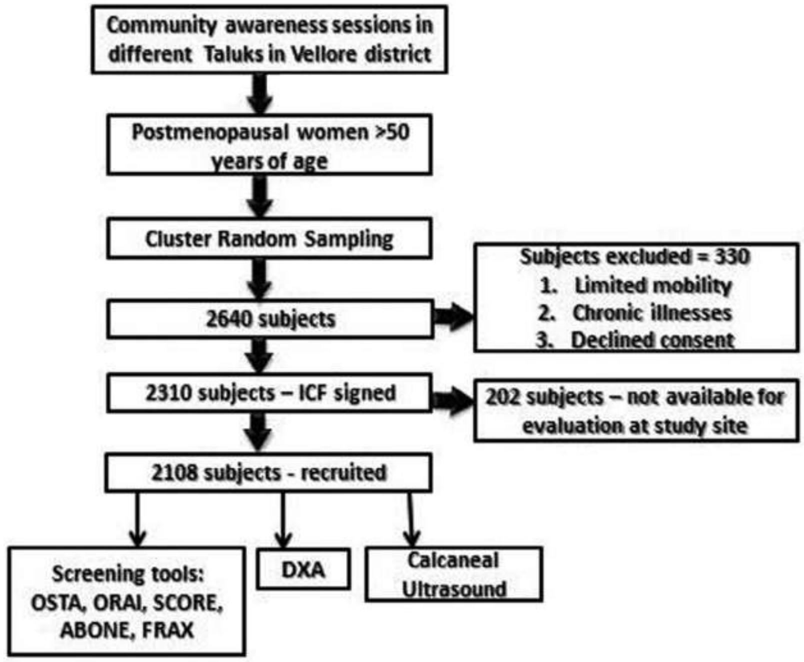

Fig. 1. Flowchart showing patient recruitment into the study. ABONE, age, bulk, one or never estrogen; DXA, dual-energy X-ray absorptiometry; FRAX®, Fracture Risk Assessment Tool; ICF, Informed Consent Form; ORAI, Osteoporosis Risk Assessment Instrument; OSTA, Osteoporosis Self-Assessment Tool for Asians; SCORE, Simple Calculated Osteoporosis Risk Estimation.

presence of rheumatoid arthritis, history of fractures, age, weight, and the use of estrogen therapy. ABONE was used in 1610 postmenopausal women and used age, weight, and the use of estrogen therapy. ORAI was more categorical and used the parameters of age, weight, and estrogen therapy, and was first validated in the Canadian multicenter osteoporosis study with 926 women aged more than 45 yr. OSTA was developed in 860 postmenopausal Asian women in 8 countries (China, Taiwan, Hong Kong, Korea, Malaysia, Singapore, Thailand, and the Philippines). OSTA was calculated as one-fifth of the difference between weight in kilogram and age in years. FRAX® was developed at the University of Sheffield as a screening tool to predict the risk of fractures. FRAX® integrates the clinical risk factors with BMD at the FN. In the present study, FRAX® was used without BMD. Body weight was measured on a calibrated weighing scale, and height was measured using a wall-mounted stadiometer. These risk assessment tools have been validated in the west in various studies.

Statistical Analysis

Demographic variables were tabulated as mean and SDs. The sensitivity, the specificity, and the area under the receiver operating characteristic (ROC) curve of each screening tool were estimated. The primary objective of the present study was to assess the performance characteristics of 6 internationally validated screening tools for osteoporosis.

Results

A total of 2108 subjects were included in the study (Fig. 1). Their baseline characteristics are shown in Table 1. The mean (SD) age of the study subjects was 60.9 (7.6) yr. The mean (SD) weight was 59.9 (12.2) kg, and the mean (SD) BMI was 26.0 (4.9) kg/m^2.

Osteoporosis at the FN was seen in 27%. In our study, we chose the following cutoffs of ≥9 for SCORE, ≥1.5 for

Table 1
Baseline Characteristics

Parameters	Mean ± SD
Age (yr)	58.5 ± 9.5
Height (m)	1.51 ± 0.06
Weight (kg)	60.2 ± 12.4
Body mass index (kg/m^2)	26.0 ± 7.1
Femoral neck BMD (g/cm^2)	0.654 ± 0.11
Calcaneal QUS—speed of sound (m/s)	1504.3 ± 31.8
Risk factors	Number (%)
History of previous fracture	126 (6)
History of rheumatoid arthritis	42 (2)
History of estrogen use	Nil

Abbr: BMD, bone mineral density; QUS, quantitative ultrasound; SD, standard deviation.

Table 2
Sensitivity and Specificity of the Screening Tools (With Cutoffs Used)

Risk assessment tool	Cutoffs used	Sensitivity (%)	Specificity (%)	AUC	95% CI
SCORE	≥9	91.3	36	0.806	0.772–0.881
ABONE	≥1.5	91	33.5	0.721*	0.691–0.743
OSTA	≤1	88.5	41.7	0.766*	0.740–0.784
ORAI	≥12	81	52	0.713*	0.682–0.736
FRAX®	≥0.7	72.7	60.5	0.736*	0.716–0.762
QUS	≤-3.7	81.9	50.3	0.730*	0.652–0.742

Abbr: ABONE, age, bulk, one or never estrogen; AUC, area under the curve; CI, confidence interval; FRAX®, Fracture Risk Assessment Tool; ORAI, Osteoporosis Risk Assessment Instrument; OSTA, Osteoporosis Self-Assessment Tool for Asians; QUS, quantitative ultrasound; SCORE, Simple Calculated Osteoporosis Risk Estimation.
*$p \leq 0.01$ for comparison of AUC of SCORE with other screening tools.

ABONE, ≤1 for OSTA, ≥12 for ORAI, ≤−3.7 for QUS, and ≥0.7% for 10-yr hip fracture risk for FRAX® based on the sensitivity and the specificity obtained for these tools.

The sensitivity and the specificity of the indices with the appropriate cutoff points and the area under the ROC curve are shown in Table 2 and in Fig. 2.

The sensitivities of SCORE, ABONE, OSTA, ORAI, FRAX®, and QUS were 91.3%, 91.0%, 88.5%, 81.0%, 72.7%, and 81.9%, and the specificities were 36.0%, 33.5%, 41.7%, 52.0%, 60.5%, and 50.3%, respectively for FN osteoporosis. When the ROCs were constructed, the area under the curve (AUC) was good only for SCORE (0.806), and the performance of the rest was under fair category (0.713–0.766). The AUCs of the other risk assessment tools were 0.721 for ABONE, 0.713 for ORAI, 0.766 for OSTA, 0.730 for QUS, and 0.736 for FRAX®. The AUC was significantly higher when compared with other screening tools ($p < 0.01$).

Discussion

The present study attempted to analyze the performance of various screening tools in predicting the risk of osteoporosis in about 2000 rural postmenopausal women. The use of SCORE was found to predict osteoporosis, with 91.3% sensitivity and a discriminatory power of 0.8. The performance of the other indices like OSTA, ABONE, and ORAI was fair. FRAX® has been validated as a tool to predict the risk of developing fractures, but was found to have a poor sensitivity in detecting osteoporosis in this study population.

Screening tools in detecting osteoporosis are inexpensive *(20)*, rapid, and easy to perform, and can be utilized in an outpatient or community-based setting. This assumes importance in a rural setting, where access to DXA scanners is limited, and the costs involved are prohibitive. The International Osteoporosis Federation recommends that there should be 10.6 DXA machines for 1 million populations. India falls far below these standards, and this impediment assumes greater proportions in a rural setting.

The performance of SCORE in our study population was similar to those in other studies published in the literature *(21)*. Studies by Lydick et al (n = 207) and Mauck et al (n = 202) have reported good sensitivities of more than 90% *(13,22)*. The use of OSTA was shown to have sensitivities ranging from 65% to 85% in previous studies *(12,15)*. The use of ORAI was promising with a sensitivity of more than 90% in the study done by Cadarette et al *(16)*. The lower sensitivity of ORAI noted in our study was probably due to the differing demographic characteristics of our population. ABONE has fewer parameters when compared with SCORE; however, the studies that have utilized ABONE as a screening tool have reported sensitivities ranging from 73% to 83% as opposed to 91% seen in our current study. We also found that QUS did not perform better than the other screening tools in predicting osteoporosis at FN. In a study by Dane et al with 351 pre- and postmenopausal women, calcaneal ultrasound weakly predicted osteoporosis at any skeletal site. The AUC ranged from 0.54 to 0.62 in the same study *(23)*.

The finding of poor sensitivity for FRAX® in the diagnosis of osteoporosis has been shown in previous studies by Daswani et al *(24)* and Bhat et al *(25)*. The performance of FRAX® was suboptimal probably because it was devised to predict fractures rather than osteoporosis. Based on our study, we found that at a cutoff of ≥0.7%, FRAX® had a sensitivity of 72.7% and an acceptable specificity.

Thus, the use of simple screening tools for the detection of osteoporosis helps in the early identification of women at risk of fractures. A timely initiation of treatment in the form of bisphosphonates *(26)* will aid in reducing the risk of sustaining fractures and alleviate the morbidity associated with them.

Our study had several strong points. Firstly, it was a community-based study that recruited more than 2000 women. Thus, our results may be applicable to a large population. Secondly, these tools may be used for mass screening of women in the rural setting. Many elderly women in rural India are confined to their homes and do not seek medical aid in time.

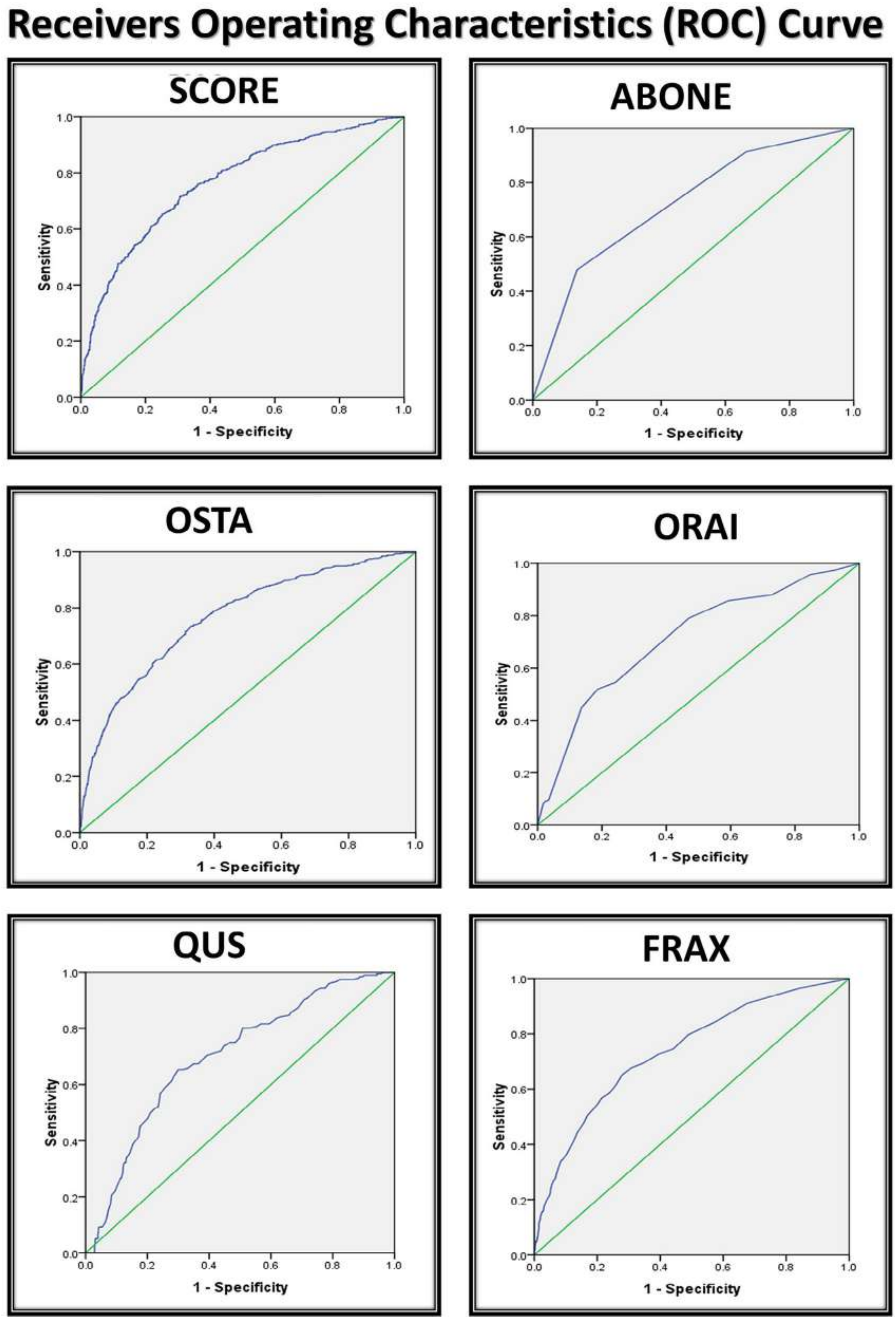

Fig. 2. ROC curves showing the performance of the various risk assessment tools. ABONE, age, bulk, one or never estrogen; FRAX®, Fracture Risk Assessment Tool; ORAI, Osteoporosis Risk Assessment Instrument; OSTA, Osteoporosis Self-Assessment Tool for Asians; QUS, quantitative ultrasound; ROC, receiver operating characteristic; SCORE, Simple Calculated Osteoporosis Risk Estimation.

The use of simple, easily available, and inexpensive tools like those used in our study will help in the triage of those at risk and assist in referral to higher centers. Thirdly, as these tools do not involve the use of sophisticated technology or technical expertise, they can be administered even by the village health worker to identify women at risk.

A few limitations of our study were that follow-up data on the occurrence of fractures in this community are not available. It would be helpful to know the incidence of fractures in the low-risk group and thus identify additional risk factors that were contributory. Also, as individuals with paralytic illness, prolonged immobilization, and malignancy were excluded, the prevalence of osteoporosis was probably underestimated. This study focused on rural postmenopausal women and cannot be generalized to the entire community.

In conclusion, in our present study, SCORE was found to be potentially applicable to identify postmenopausal women at risk of osteoporosis. Further prospective studies will need to be conducted to determine the outcome of early screening and referral in terms of fracture risk reduction. Thus, this tool may be used in resource-limited countries to screen the population at risk and to enable treating physicians to make appropriate management decisions.

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