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ORIGINAL ARTICLE

Selecting men for bone densitometry: performance of osteoporosis risk assessment tools in Portuguese men

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Abstract
Summary Clinicians need tools to identify patients most likely to benefit from bone mineral density (BMD) testing, for which cost–effectiveness does not allow generalized screening. This study supports the utility of osteoporosis risk assessment tools in selecting men for BMD testing. Different cutoff values may be appropriate for different countries and/or ethnic origins.
Introduction Our aim was to evaluate the utility of three osteoporosis (OP) risk assessment tools in a large group of Portuguese men aged 50 or more and to determine the best cutoff value to be used for selecting men for bone densitometry.
Methods We assessed the performance of three simple tools in 202 randomly selected men: body weight criterion (BWC), osteoporosis self-assessment tool for Asians (OSTA), and a modified version of the OSTA equation (OST). Previously published cutoff values (validated in postmenopausal women) and three additional cutoff values were tested. Sensitivity (SE), specificity (SP), predictive values, and area under the receiver operating characteristic (AUROC) curve for correctly selecting men with OP (defined by BMD testing) were determined.
Results Mean age of the cohort was 63.8 years. According to the World Health Organization diagnostic categories, 16.8% had osteoporosis. The best performing cutoffs for correctly selecting men with OP for BMD testing were OST<3 (SE=75.5%, SP=50.0%, AUROC=0.632), OSTA<3 (SE=73.5%, SP=58.3%, AUROC=0.659), and BWC<75 kg (SE=73.5%, SP=61.3%, AUROC=0.674).
Conclusions OP risk assessment tools seem to be useful in men aged 50 or more. Best cutoff values are different from those recommended for postmenopausal women. Different cutoff values may be appropriate for different countries and/or ethnic origins.

Keywords Densitometry · Mass screening · Men · Osteoporosis · Portugal · Risk assessment

Introduction

Osteoporosis continues to be an underrecognized problem in men, and it still goes untreated in the majority of men even in the presence of fractures. One in five men over the age of 50 years will experience an osteoporosis-related fracture in their lifetime [1]. Of all osteoporotic fractures, hip fractures contribute to the greatest morbidity, as well as mortality, both of which are greater in men than in women [2, 3]. With the increasing longevity of men, osteoporosis in this gender will soon become an even greater burden to society and health care systems worldwide. It has been estimated that by the year 2040, there will be as many hip fractures worldwide in men as was seen in women in the year 2000 [4].

Many well-controlled prospective studies with dual-energy X-ray absorptiometry (DXA), particularly in elderly women, indicate that the risk of fracture about doubles for each standard deviation (SD) reduction in bone mineral density (BMD) [5]. BMD measurements can be useful in several ways, including contributing to the diagnosis of skeletal fragility, gauging its severity, and guiding decisions concerning therapy.

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There is a progressive tendency to recommend the identification of individuals for treatment based on a comprehensive fracture risk assessment rather than BMD status alone. A fracture risk assessment tool (FRAX™) [6] has recently been developed based on the use of clinical risk factors with or without BMD. However, the importance of the World Health Organization (WHO) categories in the decision making remains high, and clinicians will still have to face the question about which individuals to select for DXA measurements. This question is also implicit when considering (or not) the incorporation of BMD in the previously mentioned fracture risk equation.

Screening for osteoporosis with bone density measures has been recommended for men over 70 years [7, 8] and is worth further evaluation as a strategy. However, a recent cost–effectiveness analysis supported generalized screening only in those over 80 years, as well as in men over the age of 65 years who have previously experienced a fracture [9]. DXA is readily available, there are well-developed reference data for its use, and DXA BMD levels are strongly related to fracture risk in men [10, 11]. Moreover, pharmacological therapies appear to be effective in men chosen on the basis of low DXA BMD levels [12–15]. For all these reasons, DXA must be considered the first choice for assessing bone strength in men, but cost and effectiveness does not allow for generalized screening and advises the use of some selection of the target population.

Reviews about the clinical applications of bone densitometry suggest that clinicians need tools to identify patients most likely to benefit from DXA testing [16, 17]. A simple risk assessment tool may also have value for increasing the awareness of osteoporosis and for encouraging more efficient use of BMD measurements, that is, in patients who have a higher probability of low BMD, especially in otherwise healthy, asymptomatic patients. Several studies have examined and confirmed the ability of individual risk factors to identify postmenopausal women likely to have osteoporosis and some have proposed simple composite tools obtained by questionnaire and based on a score [3, 18–27]. The purpose of these risk assessment indices is not to diagnose osteoporosis or low BMD but to identify people who are more likely to have low BMD and should, therefore, be submitted to DXA. The easier to use in clinical practice are certainly the osteoporosis self-assessment tool [3, 27] and the body weight criterion [19]. They have been validated for women of diverse origins, including Asian and Caucasian [3, 28–32]. The evidence for the utility of these rules in a clinical setting is scarce and few studies have been performed in men [33–40]. Their utility is not necessarily the same in males and females and in different populations, as the contribution of osteoporotic factors may vary.

Therefore, we aimed to assess the validity and to establish the best cutoff values for the OSTA, OST, and BWC criteria in men, using a large group of randomly selected Portuguese males aged 50 or more.

Materials and methods

Data collection

Data collection took place in Santo António dos Olivais (SAOL), Coimbra, Portugal, in the years of 1998 and 1999. The methodology has been previously described [41]. This county has a mixture of rural and urban population, which presents epidemiological patterns of age and gender distribution, income, and consumer habits considered to be similar to those of the general Portuguese population. It has about 25,000 inhabitants. Residents were randomly selected from the 19,000 registered voters following a computer-generated random number list, stratified to gender and 5 year age groups. People were invited to participate by mail explaining the nature and purposes of the study. There were no exclusion criteria. Nonrespondents were contacted a second time. We aimed at a total of at least 1,600 participants. A total of 6,000 invitations were sent out before this number was reached; 1,100 letters bounced back due to change in address, death, and other reasons. Altogether, 1,745 accepted to participate.

Participants responded to a comprehensive questionnaire regarding risk factors for osteoporosis in personal and family history. Height and weight were recorded. DXA scans of the spine and proximal femur were performed, using a Hologic QDR 4500/c bone densitometer. Scans were performed and analyzed according to the manufacturer's instructions. Seventy-three participants were excluded from final analysis due to incomplete data or unresolved technical difficulties in the DXA scan. A total of 1,706 participants were studied (1,233 women and 473 men). For the purposes of this study, all men aged 50 or more were included (study cohort=202).

Calculating decision algorithm scores

Based on a critical review of the literature, with consideration of published performance indicators and simplicity, we selected three simple decision algorithms to test: the body weight criterion (BWC) [19], the osteoporosis self-assessment tool for Asians (OSTA) [27], and a modified version of the OSTA equation (OST) [3, 27]. Their scoring methods, with previously validated selection cutoff points in postmenopausal women, are presented in Table 1. All the information needed were available in the SAOL database. Age was calculated to the date of the DXA scan.

Table 1 Three simple decision rules for bone mineral density testing among postmenopausal women

Body weight criterion, test if
Weight<70 kg
Osteoporosis self-assessment tool for Asians, test if score<2
0.2×body weight in kilograms (truncate to yield an integer)−0.2× age in years (truncate to yield an integer)
Osteoporosis self-assessment tool, test if score<2
0.2×(body weight in kilograms−age in years), truncate to yield an integer

Gold standard

BMD values as assessed by DXA were used as the gold standard for diagnosing osteoporosis. We used the WHO thresholds to classify our patients into three diagnostic categories: normal (T-score≥−1.0 SD), osteopenic (−1.0> T-score>−2.5 SD), or osteoporotic (T-score≤−2.5 SD). The young normal reference values used for the calculation of T-scores were National Health and Nutrition Examination Survey III reference for the hip [42] and the HOLOGIC male Caucasian reference database for the spine. In each case, the lowest BMD T-score at the lumbar spine (L1–L4), femoral neck, or total hip was considered.

Statistical analysis

Descriptive characteristics of the study population were tabulated as means and SD, or proportions as applicable. Differences among groups of patients were calculated by analysis of variance or chi-square test as applicable. Pearson's correlation coefficient was used to assess the relationship between age and T-score values. Significance was determined using a two-sided α level of 0.05.

The sensitivity, specificity, positive predictive value, negative predictive value (NPV), and the area under the receiver operating characteristic (AUROC) curve of each decision algorithm for selecting men with osteoporosis by BMD testing were determined.

Sensitivity was defined as the proportion of men with osteoporosis (T-score≤−2.5 SD) who tested positive on the decision algorithm (indication for DXA in the binomial classification) and specificity was defined as the proportion of men without osteoporosis who tested normal on the risk assessment (having index values in the range considered low risk). Positive predictive value was defined as the proportion of men with a positive algorithm score who are actual cases of osteoporosis and negative predictive value was defined as the proportion of men with a negative algorithm result who are actual noncases of osteoporosis. The AUROC curve was used as a measure of the overall ability of each strategy to discriminate between men with and without osteoporosis. Statistical analysis was performed using SPSS 14.0 for Windows.

Results

Our study population included 202 men aged 50 to 88 years, with a mean age of 64 years. Table 2 summarizes the descriptive characteristics of the study cohort, including age distribution, WHO criteria, and T-score. The age distribution deserves attention as it includes a large number of participants with less than 70 years (75.7%), i.e., belonging to the group where a decision-aid tool is potentially more influential.

Table 3 summarizes the descriptive characteristics of the study cohort stratified on the basis of the three WHO diagnostic categories.

The overall percentage of osteoporosis at lumbar spine, femoral neck, or total hip was 16.8% (n=34). The percentage of T-score≤−2.5 at each measurement site was 14.9% at lumbar spine (n=30), 5% at femoral neck (n=10), and 1% at total hip (n=2). The percentage of men with osteoporosis increased with age from 14.4% among men aged ≥50 and <70 years (22/153) to 24.5% among men aged ≥70 years (12/49). The WHO diagnostic categories were associated with significant differences regarding weight, body mass index (BMI), and all the risk assessment tools under scrutiny (p<0.001), but not with age and height.

Because both the OSTA and OST included age as part of the decision algorithm, we further investigated the relationship

Table 2 Summary of descriptive characteristics of the study cohort (n=202)

Age (years, mean ± SD)	63.77±8.22
Age group—n (%)	
Age ≥50 and <70 years	153 (75.7)
Age ≥70 years	49 (24.3)
Height (cm, mean ± SD)	167.84±6.78
Weight (kg, mean ± SD)	76.23±10.77
Body mass index (kg/m^2, mean ± SD)	27.05±3.42
WHO diagnostic categories—n (%)[a]	
Normal	65 (32.2)
Osteopenia	103 (51.0)
Osteoporosis	34 (16.8)
T-score (mean ± SD)	
Lumbar spine	−1.1±1.4
Femoral neck	−1.05±0.86
Total hip	−0.48±0.96
OSTA score (mean ± SD)	2.52±2.87
OST score (mean ± SD)	2.18±2.59

[a] The lowest BMD T-score at the lumbar spine, femoral neck, or total hip was considered

Table 3 Summary of descriptive characteristics of the study cohort according to the three WHO diagnostic categories (n=202)

	Normal (n=65)	Osteopenia (n=103)	Osteoporosis (n=34)	p
Age (years, mean ± SD)	62.84±7.16	63.80±8.36	65.46±9.52	0.322
Age group—n (%)				0.229
Age ≥50 and <70 years (n=153)	52 (34.0)	79 (51.6)	22 (14.4)	
Age ≥70 years (n=49)	13 (26.5)	24 (49.0)	12 (24.5)	
Height (cm, mean ± SD)	169.29±6.49	167.45±6.72	166.26±7.19	0.075
Weight (kg, mean ± SD)	81.2±9.24	74.88±10.78	70.84±9.89	<0.001
BMI (kg/m^2, mean ± SD)	28.34±2.90	26.68±3.44	25.66±3.56	<0.001
OSTA score (mean ± SD)	3.75±2.62	2.25±2.73	1.00±2.90	<0.001
OST score (mean ± SD)	3.25±2.37	1.92±2.51	0.91±2.54	<0.001

The lowest BMD T-score at the lumbar spine, femoral neck, or total hip was considered

between age and T-scores. We found a significant correlation between age and femoral neck (r_p=−0.26; p<0.001) and total hip (r_p=−0.19; p=0.008) T-scores but not between age and lumbar spine T-score (r_p=0.06; p=0.397). These results likely reflect the fact that the spine BMD is often increased by degenerative changes in the unselected elderly population.

Table 4 shows the sensitivity, specificity, predictive values, and AUROC curve of each decision rule for selecting men with osteoporosis in the study cohort. Maximum sensitivity (85.3% for OST, 76.5% for OSTA, and 82.4% for BWC) was achieved with the highest cutoffs (OST/OSTA<4 and BWC<80 kg), but at the cost of very low specificities (32.7% for the OST, 42.9% for the OSTA, and 35.7% for the BWC), resulting in a larger number of unnecessary DXA scans.

Best AUROC curves were for OST<3 (AUROC=0.632), OSTA<3 (AUROC=0.659), and BWC<75 kg (AUROC=0.674). Sensitivities at these cutoffs were 76.5% for the OST, 73.5% for the OSTA, and 73.5% for the BWC. Negative predictive value, an important characteristic for the purpose of this work, was also quite high at these cutoffs—91.3% for OST, 91.6% for OSTA, and 92% for BWC.

Comparison was also made with the age criterion and several age cutoffs were tested (≥60, 65, 70, 75, and 80 years old). AUROC curves had bad performances and the 95% confidence intervals (CIs) included 0.5 for all of them, suggesting that they do not have enough discriminative power to select men for BMD.

Discussion

There are three recommended steps in developing and testing tools to aid clinical decision making: development, validation in several cohorts, and impact assessment. Information on

Table 4 Percentage of men selected for DXA, SE, SP, PPV, NPV, and AUROC curve of each algorithm and for different cutoffs, for correctly selecting men with osteoporosis in the study cohort (n=202)

	% of men selected	SE, %	SP, %	PPV, %	NPV, %	AUROC (95% CI)
OST<1	30.7	47.1	72.6	25.8	87.1	0.598 (0.490–0.707)
OST<2	40.6	61.8	63.7	25.6	89.2	0.627 (0.524–0.731)
OST<3	54.5	76.5	50.0	23.6	91.3	0.632 (0.535–0.730)
OST<4	70.3	85.3	32.7	20.4	91.7	0.590 (0.492–0.688)
OSTA<1	21.3	38.2	82.1	30.2	86.8	0.602 (0.491–0.713)
OSTA<2	36.1	55.9	67.9	26.0	88.4	0.619 (0.513–0.724)
OSTA<3	47.0	73.5	58.3	26.3	91.6	0.659 (0.562–0.757)
OSTA<4	60.4	76.5	42.9	21.3	90.0	0.597 (0.497–0.697)
BWC<65	13.4	26.5	89.3	33.3	85.7	0.579 (0.467–0.691)
BWC<70	26.7	47.1	77.4	29.6	87.8	0.622 (0.514–0.731)
BWC<75	44.6	73.5	61.3	27.8	92.0	0.674 (0.577–0.771)
BWC<80	67.3	82.4	35.7	20.6	90.9	0.590 (0.492–0.689)
Age≥60 years	61.9	61.8	38.1	16.8	83.1	0.499 (0.393–0.606)
Age≥65 years	40.1	52.9	62.5	22.2	86.8	0.577 (0.471–0.684)
Age≥70 years	24.3	35.3	78.0	24.5	85.6	0.566 (0.457–0.676)
Age≥75 years	9.9	26.5	93.5	45.0	86.3	0.600 (0.486–0.713)
Age≥80 years	3.5	5.9	97.0	28.6	83.6	0.515 (0.406–0.623)

BMD T-score≤−2.5 by lowest value at the lumbar spine, femoral neck, or total hip was considered. Note: previously validated cutoff values in postmenopausal women—OST<2, OSTA<2, and BWC<70 kg. Comparison is also made with the age criterion

SE sensitivity, *SP* specificity, *PPV* positive predictive value, *NPV* negative predictive value

their utility in different populations is especially important in order to establish the generalizability of these approaches and to assure their validity in clinical practice as applied in different clinical and epidemiological settings [21].

We analyzed the value of three simple decision algorithms for selecting men for BMD in 202 Portuguese men aged 50 or more; mean age was 64 years and the prevalence of osteoporosis was quite high in our population (16.8%), highlighting the need for reliable screening tools for the identification of men at risk for osteoporosis.

Compared to the majority of previous reports, this study had the virtue of not being retrospective. It was a cross-sectional study, performed in a nonclinical setting and in a random population. Such results are more probably generalizable than if the sample had been submitted to imprecise preselection. Because the study sample was randomly selected with no clinical exclusion criteria, we cannot be sure that all osteoporotic patients had primary osteoporosis; however, the prevalence of known secondary causes of osteoporosis in our sample was very small, and this aspect probably has very little effect on the value of our study. Our population had a wide representation in terms of age, height, weight, and BMD status (Table 2).

An important point of this study is the high proportion of men aged <70 years (75.7%). Indeed, this is the group where decision-aid tools are especially needed. In fact, several authorities (including Portuguese) recommend that BMD testing should be performed in all men aged more than 70 years regardless of additional risk factors [7, 8]. Several age criterions were tested in our study and all of them showed low discriminative power to select men for BMD. Among the 34 men who had osteoporosis, only 12 (35.3%) were aged 70 or more. The majority of osteoporosis cases would be missed if this cutoff alone was used as a criterion for selecting men for BMD.

The representativeness of our sample is further supported by the association between WHO status, weight, and BMI (Table 3) and by the correlation between femoral neck and total hip T-scores and age. The relationship between WHO status and the algorithms tested here is also clear.

Ideally, one screening test should be 100% sensitive and 100% specific. However, in practice, this does not occur: Sensitivity and specificity are usually inversely related. A test with good sensitivity is favored when a false-negative result is more prejudicial for the patient than a false-positive one (curable disease, early diagnosis associated with better prognosis) or when the disease is uncommon. A test with a good specificity is favored when a false-positive result is more prejudicial for the patient than a false-negative one (aggressive treatment, incurable disease, etc.).

Because there is no risk of harm to the patient from unnecessary treatment or invasive diagnostic testing in case of a false-positive result from the OST, OSTA, or BWC and also because treatment for low BMD would only be initiated upon confirmation by DXA, a safe and noninvasive diagnostic procedure, more importance has to be given to sensitivity rather than specificity. However, specificity must be contained at reasonable levels in order to reduce unnecessary testing and costs for the community and the patient.

Simplicity is also of crucial importance to foster the implementation of any screening tool and its impact in practice. In this study involving white men aged 50 years or more, using a cutoff of OST/OSTA<3 or BWC<75 kg, most men with osteoporosis were successfully identified, with a sensitivity of 76.5% for the OST, 73.5% for the OSTA, and 73.5% for the BWC. At these cutoffs, specificity was 50.0% for the OSTA, 58.3% for the OST, and 61.3% for the BWC. In other words, the OST and OSTA, based only on age and weight, and BWC, based on weight alone, permit identifying men at low risk of osteoporosis who would not need DXA testing (respectively, 91.3%, 91.6%, and 92% of patients classified as low risk with OST, OSTA, and BWC do not have osteoporosis).

The use of a cutoff of OST/OSTA<2 or BWC<70 kg would represent unacceptable losses in terms of sensitivity (61.8% for the OST, 55.9% for the OSTA, and 47.1% for the BWC) while the use of a cutoff of OST/OSTA<4 or BWC< 80 kg would represent unacceptable losses in terms of specificity (32.7% for the OST, 42.9% for the OSTA, and 35.7% for the BWC), without relevant gains in terms of sensitivity or NPV (for the OSTA and BWC, it would even represent a loss in terms of NPV).

The above considerations have their reflection in the AUROC curves (a measure of test accuracy), the cutoff of OST/OSTA<3 and BWC<75 kg yielding the best discriminatory performances—0.632 (95% CI, 0.535–0.730) for the OST, 0.659 (95% CI, 0.562–0.757) for the OSTA, and 0.674 (95% CI, 0.577–0.771) for the BWC.

Hochberg et al. [33] applied the OST index to two large groups of men in Rotterdam and Baltimore. They found that the OST predicted osteoporosis as measured by DXA, using cutoffs similar to postmenopausal women (OST<2) and reported a sensitivity and specificity of 79% and 51%, respectively, for the Rotterdam study and 88% and 32% for the Baltimore cohort. Adler et al. [34] used a multi-ethnic sample of men extracted from pulmonary and rheumatology clinics at an American veteran's hospital and using a cutoff of OST<3, obtained a sensitivity of 93%, and a specificity of 66%. Kung et al. [35], in a large sample of Chinese men, validated the OST using a different cutoff (OST<0), with a sensitivity of 81% and specificity of 66%. Ghazi et al. [36], in a cohort of Moroccan men seen at an outpatient rheumatology center and using a score of OST<2, found that sensitivity was 64.0% and specificity was 60.3% for OP at any given BMD measurement site. Sinnott et al. [37]

conducted a study in a cohort of African American males aged 35 or older, and using a cutoff value of OST<4, they predicted low bone mass (defined as a T-score of −2 or less at the total hip, femoral neck, or trochanter) with a sensitivity of 83% and a specificity of 57%; using the cutoff value of BWC<85 kg, they predicted low bone mass with a sensitivity of 74% and a specificity of 50%. Skedros et al. [38] found OST to be a useful osteoporosis screening tool in a population of 158 nonhospitalized white men (mean age 67.5 years), reporting a sensitivity of 85% and a specificity of 64% for an OST score<2. On the other hand, in a study by Perez-Castrillon et al. [39], an OST cutoff of 2 was not useful (sensitivity of 39%, specificity of 86%, and a nonsignificant AUROC curve) in a population of 67 Spanish men referred due to lumbar pain or suspected osteoporosis (mean age 51 years). In the largest-scale evaluation of osteoporosis screening tools (4,658 US Caucasian men and 1,914 Hong Kong Chinese men), published by Lynn et al. [40], OST was useful in both populations, with a sensitivity of 87.6% and a specificity of 36.1% for Caucasians and a sensitivity of 91.4% and a specificity of 36.4 for Chinese, when using a cutoff≤2 for Caucasians and a cutoff≤−1 for Chinese.

Differences between studies highlight the importance of assessing osteoporosis screening tools in different populations and the need to define appropriate cutoffs for each population. These reported differences may be explained by selection of the population, demographic differences (namely age), and ethnical and racial differences regarding body size, composition, and BMD measurements. In our population, the prevalence of osteoporosis in the femoral neck and hip is quite low in comparison to the spine. This probably reflects the relative youth of the men with 75.7% being younger than 70 as cortical bone loss tends to occur later. The very low prevalence of osteoporosis in femoral neck and hip may contribute to the finding that body weight was a better predictor of bone density than indices based on weight plus age.

Our results must be interpreted in the light of several limitations: First, we did not test all decision algorithms that have been published, rather excluding more complex formulas. Self-selection of volunteers biased our population sample toward higher levels of education and income (data not shown). However, the impact of such deviations on the evaluation of the performance of theses indices is probably minor, as they are designed for application in practice without consideration of other factors.

The practical application of these decision rules and risk indices in facilitating clinical decisions and promoting rational use of resources should be explored further, including all potential benefits as well as harms, such as those derived of labeling men at high risk for osteoporosis [43]. The use of such algorithms should not preclude due to consideration of other less common but important risk factors. Men with a prior fragility fracture are at high risk for osteoporosis and recurrent fracture and should be referred for BMD testing to facilitate treatment decisions, irrespective of other considerations [44, 45]. Similarly, men with major risk factors for secondary osteoporosis should discuss bone health and BMD testing independent of these decision rules [46].

A larger population-based study would be valuable to assure the scientific reliability of our findings and a direct comparison with usual clinical practice would also be valuable to determine if decision rule approaches provide more optimal use of BMD testing [47].

In summary, we tested three risk tools at four different cutoffs and found that results were better for the OST/OSTA<3 and BWC<75 kg. Our results confirm the validity of the OST, OSTA, and BWC to support physicians and public health authorities to focus DXA testing on individuals at increased risk of osteoporosis, thus increasing its cost–effectiveness. With BWC being the simplest one and having a statistical performance that is similar to the others, our data strongly support the use of body weight as the preferred method to select men for DXA scanning.

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Conflicts of interest None.

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