The Discriminatory Capacity of BMD Measurements by DXL at the Calcaneus and DXA at the Hip and Spine Including Clinical Risk Factors to Detecting Patients with Vertebral Fractures

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C. Muschitz, H. P. Dimai, R. Kocijan, A. Kaider, H. Resch

Abstract: Purpose: Osteoporotic fracture risk depends on bone mineral density (BMD) and clinical risk factors (CRF). DXA of spine/hip is considered gold standard for BMD assessment, but due to degenerative conditions particularly among the older population, assessment of BMD at the lumbar spine has been shown to be of limited significance. Portable calcaneal DXL (dual X-ray technology and laser) can be an easily obtainable alternative.

Methods: Vertebral fractures were evaluated in a baseline analysis of 588 females and males (median age 64.4, range 17.6–93.1 years) comparing BMD measurements by DXL or DXA and CRF with/without BMD. 160 had radiologically verified vertebral fractures. Area under the ROC curves (AUC) were calculated.

Results: AUC for detection of vertebral fractures was comparable for DXL at calcaneus and DXA at femoral neck (DXL 0.665, DXA 0.670). Odds ratio for prevalent vertebral fracture was generally weak for DXA femoral neck (0.613) and DXL (0.521). Combining BMD and CRF, a prognostic improvement in case of DXA at femoral neck (AUC 0.696, p = 0.02), DXL at calcaneus (AUC 0.699, p = 0.059), and DXA at total hip (AUC 0.861, p = 0.06) was observed.

Conclusions: DXL was similarly sensitive compared with DXA for identification of subjects with vertebral fragility fractures, and combination of CRF with BMD by DXL or DXA further increased the discriminatory capacity for detection of patients susceptible to vertebral fracture.

Key words: vertebral fractures, DXA spine/hip, DXL calcaneus, clinical risk factors


Methoden: In dieser Studie wurden an 588 unbehandelten Frauen und Männern (mittleres Alter 64,4, Altersspanne 17,6–93,1 Jahre) am gleichen Tag sowohl mittels DXA-Technik die BMD der Hüfte/LWS als auch mittels DXL die BMD am Kalkaneus bestimmt. Zusätzlich wurden die CRF erhoben. 160 Patienten hatten radiologisch verifizierte Wirbelkörperfrakturen. Zur Bestimmung der Sensitivität und Spezifität wurden AUC-Kurven („area under the ROC curves“) berechnet.

Resultate: Die AUC zum Nachweis von vertebrealen Frakturen war für DXA am Schenkelhals und für DXL am Kalkaneus vergleichbar (DXL 0.665, DXA 0.670). Die AUC für CRFs ohne BMD-Messungen war mit einem Wert von 0.805 deutlich den alleinigen BMD-Messungen überlegen. Die Kombination von BMD und CRF führte zu einer Verbesserung der prognostischen Vorhersage: DXA Schenkelhals und CRF: AUC 0.869, p = 0.002; DXL Kalkaneus und CRF: AUC 0.869, p = 0.059.


Schlüsselwörter: vertebrale Frakturen, DXA Wirbelsäule/Hüfte, DXL Kalkaneus, klinische Risikofaktoren

Introduction

An increasing median age of populations worldwide is responsible for a major increase in the incidence of osteoporosis and its consequences in postmenopausal women and men [1]. Despite its prevalence, osteoporosis is frequently diagnosed with delay and many patients still remain untreated. Underdiagnosis of vertebral fractures is a worldwide problem and the proportion of these fractures in females and males that go unrecognized is up to 30–45%. Furthermore, clinically diagnosed thoracic or lumbar vertebral fractures can be regarded as a risk factor for subsequent, long-term morbidity in women and for mortality and increased fracture incidence in both genders [2–4].

Low bone mineral density (BMD) is a strong predictor of fragility fractures [5–7]. Dual-energy X-ray absorptiometry (DXA) of the spine and hip is considered gold standard for assessment of BMD and diagnosis of osteoporosis according to the WHO criteria. Clinical assessment of fracture risk should depend on the presence of clinical risk factors (CRF) and BMD values [8].

Alternative methods such as BMD measurement of the calcaneus, which would be less prone to degenerative alterations, would offer an attractive alternative [9]. Calcaneal bone is similar in structure to the vertebrae and it consists mainly of trabecular bone (up to 90%) [8]. In comparison to conventional DXA, the DXL device (Calscan® DXL) is a portable trolley, easy to use, and less expensive. In addition, these measurements are less time-consuming (taking about one minute), effective radiation dose is low (< 0.2 µSv), and even immobile patients or patients with problems in positioning the hip can be scanned. Consequently, misclassification of bone and soft tissue can be reduced. Several studies suggest that BMD measurements with Calscan® DXL may well reflect the actual bone status [9–13].

A distinction should be made between the diagnosis of osteoporosis solely based on BMD and the assessment of future frac-
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ture risk. In addition, some clinical risk factors (CRF) provide extra information to BMD and could, therefore, be used to enhance risk prediction with BMD. CRF are an integral part of a calculation tool which has been developed to assess an individual 10-year fracture risk (FRAX®) for categorising individuals into risk groups according to their individual fracture risk and setting intervention thresholds [14, 15].

The hypothesis of this study was to test if BMD measurements of different skeletal sites and through different techniques have different abilities to discriminate between subjects with osteoporosis and/or prevalent osteoporotic vertebral fractures.

Objectives

The aim was to investigate the impact of CRF alone or in combination with DXA and DXL measurements on the capacity of detecting these patients.

The primary objectives of this study were to compare the ability of two different techniques of BMD measurements (DXA and DXL) by ROC curves at different skeletal sites with regard to sensitivity and to identify patients with vertebral fractures.

Secondary objectives were the calculation of ROC curves of clinical risk factors with or without BMD measurements at different skeletal sites and the identification of significant CRF in our study population.

Methods

Patients

Between July 2009 and June 2010, 2789 Caucasian outpatient female (n = 2287) and male (n = 502) subjects were referred for evaluation of osteoporosis to a specialised tertiary referral bone centre in Vienna, Austria. In this manuscript, baseline characteristics of the study population of a pre-planned 5-year follow-up study are presented. Patients with high-trauma fractures, premenopausal women, patients with malignancies, or immobile individuals were excluded from the analysis as well as subjects who had previously received any specific osteoporosis treatment except calcium and/or vitamin D. All subjects had a complete clinical work-up, including medical history, spinal X-ray (anterior-posterior + lateral), and laboratory testing. Furthermore, circulating serum levels of calcium, phosphorus, 25-hydroxyvitamin D, and intact parathyroid hormone (iPTH) were measured. The participant disposition is shown in Figure 1.

Clinical Risk Factors (CRF)

At baseline, CRF according to the FRAX® algorithm were collected for each individual [15].

Fractures

All patient self-reported fractures were verified by medical history and former doctor’s letters. Fragility fractures were defined as any fall from standing or lower height.

X-Ray

Digital spine X-rays scans with a special bone software application for enhanced delineation of osseal structures of each subject were assessed and vertebral fractures were evaluated by two experienced and certified radiologists using a semi-quantitative technique [16].

Assessment of BMD

BMD of total hip, femoral neck, and lumbar spine were measured using a DXA scanner (iDXA®, GE Healthcare Lunar, Madison, WI, USA). BMD assessments of the calcaneus were performed by DXL (Calscan®; Demetech AB; Taby, Sweden). Both measurements were performed consecutively by the same well-trained and International Osteoporosis Foundation/International Society for Clinical Densitometry- (IOF-ISCD-) certified technician.

The manufacturers’ reference databases on female and male Caucasian subjects were used for both devices [17].

Statistical Analyses

Comparison of age, weight, and BMI between groups of patients was performed by using a two-sample t-test. Osteoporosis was defined as T-score ≤ –2.5 SD, osteopenia as T-score ≤ –1.0 SD and > –2.5 SD. T-scores > –1.0 SD were considered as normal values for DXA and DXL. Using this classification, the McNemar test was used to test for statistically significant differences in the detection of osteoporosis.

Sensitivities, specificities, and receiver operating characteristic (ROC) curves were calculated to describe the accuracy of the BMD measurements with regard to the probability
**Table 1: (a–c)** Baseline characteristics of all patients of the analysis \( n = 588 \) including age, BMI, gender, vertebral fracture status, and BMD measurements expressed as T-scores. Detection rates for subjects with T-scores < −2.5 were higher for DXL compared with DXA spine or hip \( p < 0.0001 \).

<table>
<thead>
<tr>
<th></th>
<th>Women ( n = 494 )</th>
<th>Men ( n = 94 )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age [years], (range)</td>
<td>68.9 (17.6–93.1)</td>
<td>62.8 (25.5–90.2)</td>
</tr>
<tr>
<td>Mean BMI [g/cm²], ± SD</td>
<td>25.4 ± 5.1</td>
<td>25.5 ± 4.2</td>
</tr>
<tr>
<td>Without vertebral fracture, n ( %)</td>
<td>364 (74 %)</td>
<td>64 (68 %)</td>
</tr>
<tr>
<td>With vertebral fracture, n ( %)</td>
<td>130 (26 %)</td>
<td>30 (32 %)</td>
</tr>
<tr>
<td>1 vertebral fracture</td>
<td>72 (83 %)</td>
<td>15 (17 %)</td>
</tr>
<tr>
<td>2 vertebral fractures</td>
<td>43 (83 %)</td>
<td>9 (17 %)</td>
</tr>
<tr>
<td>≥ 3 vertebral fractures</td>
<td>15 (71 %)</td>
<td>6 (29 %)</td>
</tr>
</tbody>
</table>

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<thead>
<tr>
<th></th>
<th>DXL ( n = 588 )</th>
<th>DXA femoral neck ( n = 566 )</th>
<th>DXA total hip ( n = 569 )</th>
<th>DXA L1–L4 ( n = 539 )</th>
</tr>
</thead>
<tbody>
<tr>
<td>T-score &gt; −1.0</td>
<td>93 (16 %)</td>
<td>149 (26 %)</td>
<td>194 (34 %)</td>
<td>140 (26 %)</td>
</tr>
<tr>
<td>T-score −1.0 to −2.5</td>
<td>291 (49 %)</td>
<td>317 (56 %)</td>
<td>285 (50 %)</td>
<td>274 (51 %)</td>
</tr>
<tr>
<td>T-score &lt; −2.5</td>
<td>204 (35 %)</td>
<td>100 (18 %)</td>
<td>90 (16 %)</td>
<td>125 (23 %)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>DXL ( n = 588 )</th>
<th>DXA femoral neck ( n = 566 )</th>
<th>DXA total hip ( n = 569 )</th>
<th>DXA L1–L4 ( n = 539 )</th>
</tr>
</thead>
<tbody>
<tr>
<td>No fx</td>
<td>84 (20 %)</td>
<td>9 (6 %)</td>
<td>137 (33 %)</td>
<td>12 (8 %)</td>
</tr>
<tr>
<td>Vert fx</td>
<td>223 (52 %)</td>
<td>68 (42 %)</td>
<td>211 (51 %)</td>
<td>106 (71 %)</td>
</tr>
<tr>
<td>T-score &gt; −1.0</td>
<td>12 (8 %)</td>
<td>169 (40 %)</td>
<td>25 (17 %)</td>
<td>120 (30 %)</td>
</tr>
<tr>
<td>T-score −1.0 to −2.5</td>
<td>32 (21 %)</td>
<td>57 (14 %)</td>
<td>33 (22 %)</td>
<td>89 (22 %)</td>
</tr>
<tr>
<td>T-score &lt; −2.5</td>
<td>428 (73 %)</td>
<td>416 (74 %)</td>
<td>150 (26 %)</td>
<td>419 (74 %)</td>
</tr>
</tbody>
</table>

No fx: no vertebral fracture, Vert fx: vertebral fracture.

The Discriminatory Capacity of BMD Measurements

**Table 2:** Patient characteristics of individuals with/without vertebral fractures at baseline

<table>
<thead>
<tr>
<th></th>
<th>With vertebral fractures ( n = 160 )</th>
<th>Without vertebral fractures ( n = 428 )</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender [% female; % male]</td>
<td>81/19</td>
<td>88/15</td>
<td></td>
</tr>
<tr>
<td>Median age [years], (range)</td>
<td>74.4</td>
<td>65.7</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Mean weight [kg] ± SD</td>
<td>70.5 ± 14.7</td>
<td>67.9 ± 14.7</td>
<td>0.067</td>
</tr>
<tr>
<td>Mean BMI [g/cm²] ± SD</td>
<td>26.5 ± 5.2</td>
<td>25.0 ± 4.9</td>
<td>0.002</td>
</tr>
<tr>
<td>Clinical risk factors, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fragility fracture</td>
<td>97 (60)</td>
<td>33 (8)</td>
<td></td>
</tr>
<tr>
<td>Hip fracture of a parent</td>
<td>9 (26)</td>
<td>26 (6)</td>
<td></td>
</tr>
<tr>
<td>Currently smoking</td>
<td>18 (27)</td>
<td>49 (11)</td>
<td></td>
</tr>
<tr>
<td>Rheumatoid arthritis</td>
<td>7 (28)</td>
<td>18 (4)</td>
<td></td>
</tr>
<tr>
<td>Corticosteroids</td>
<td>6 (25)</td>
<td>18 (4)</td>
<td></td>
</tr>
<tr>
<td>Alcohol intake &gt; 3 units/day</td>
<td>10 (45)</td>
<td>12 (3)</td>
<td></td>
</tr>
<tr>
<td>Secondary osteoporosis</td>
<td>18 (27)</td>
<td>48 (11)</td>
<td></td>
</tr>
</tbody>
</table>

Figure 2: Receiver operating characteristic (ROC) curves of all BMD measurements: DXA femoral neck = 0.670, DXL calcaneus = 0.685, DXA total hip = 0.661, DXA lumbar spine = 0.598; p = 0.04 for comparison of DXA at lumbar spine and DXL at calcaneus.

Figure 3: Delineation of improvement in prediction of fracture by combination of BMD measurement with CRF according to the FRAX®; AUC for DXA = BMD femoral neck; AUC for DXL = BMD calcaneus; graphs show different BMD measurements; (A) ROC of CRF without BMD measurement, (B) ROC curves of CRF and BMD measurements (DXA femoral neck/DXL calcaneus).


**Discussion**

In the current study, DXA, the gold standard for BMD measurement, was most sensitive when measured at the femoral neck, whereas measurement at the lumbar spine had a very low ability to detect patients with vertebral fragility fractures [18–20]. In contrast to clinical studies with highly selected patients, a mixed and untreated population was recruited into this study, thus reflecting a situation of daily practice.

Using diagnostic categories as suggested by the WHO (normal BMD, osteopenia, osteoporosis) we discovered that the number of patients classified as osteoporotic was comparable among the different methods of BMD measurements. These findings are supported by previously published clinical studies on heel DXL. Therefore, calcaneal DXL might be an effective alternative to conventional DXA measurements, especially in geographical regions where DXA is not available or in situations in which DXA scans might not be feasible, eg, for immobile patients or patients with severe osteoarthroses.

Regarding the identification of subjects with prevalent vertebral fractures, low BMD determined by DXA at the femoral neck and by DXL at the calcaneus generally are superior compared to measurements at the lumbar spine. However, when BMD measurements were solely considered, their sensitivity and specificity were only moderate. Therefore, only BMD measurement, regardless of the method applied, is a not very reliable means in identifying subjects with increased vertebral fractures.

In contrast to this, presence or absence of CRF had a much higher discriminative ability compared with BMD measurements [21].

One of the limitations of this study is its retrospective design. Another limitation is the relatively small number of 588 female and male subjects included in this study. Therefore the discriminatory ability with regard to hip fractures could not be analyzed in this study, due to the low number of cases. On the other hand our population represents a homogenous collective of patients. However, a prospective study of > 4000 Swedish women demonstrated that prediction of hip fractures is feasible by calcaneal DXL [22].

Results from this study underline that BMD measurement is a necessary and useful tool in determining patients with fractures. Both DXA and DXL scans proved to provide feasible data although the detection rates for osteoporotic BMD measurements expressed as a T-score of < −2.5 were significantly higher for calcaneal DXL compared with DXA of spine or hip.

In conclusion, none of the BMD measurements alone is comparable to the discriminative power of the CRF alone. Our data demonstrate that BMD measurements by DXA at the femoral neck or DXL at the calcaneus are comparable with regard to identifying patients with prevalent vertebral fractures. Therefore DXL measurements might be a feasible, cheaper, and easily transportable alternative in regions where DXA is not available.

**Conflict of Interest**

The authors state no conflict of interest.

This study was not supported by any grant or pharmaceutical company. Vinforce receives academic funding grants.


**References:**

3. Hasserius R, Karlsson MK, Nilsson BE, et al; European Vertebral Osteoporosis Study. Prevalent vertebral deformities predict increased mortality and increased fracture rate in both men and women: a 10-year population-based study of 588 in-

≥ 3 vertebral fractures (Table 1). In general, these patients were older (74.4 [range: 37.5–93.1] vs. 65.7 [17.6–92.9] years; p < 0.0001) and had a higher body mass index (BMI; 26.5 ± 5.2 vs 25.0 ± 4.9 g/cm²; p = 0.002) compared with subjects without vertebral fractures (Table 2). Among our patients with vertebral fractures there were 130 females (81 %) and 30 males (19 %). These percentages are in line with the gender distribution of the female and male study population (84 % females vs. 16 % males). More than 60 % (97/160 patients) of all fractures were fragility fractures and not related to any adequate trauma. Clinical signs in these patients were sudden or chronically persistent back pain. Fragility fracture and alcohol intake of > 3 units per day were the most discriminating risk factors in patients with prevalent fractures.

**BMD Measurements and Detection Frequency**

Subjects with normal BMD, osteopenia, and osteoporosis were identified by BMD measurements (g/cm²) and by calculation of T-scores at different locations according to each manufacturer’s database.

Detection frequency of subjects with a T-score of < −2.5 was higher with DXL compared with DXA. These differences were statistically significant for all comparisons of DXL and DXA (p < 0.0001). The detection frequency of osteopenic subjects was comparable for all measurements.

**ROC Analysis**

For the estimation of sensitivity and specificity of calcaneal DXL and DXA at different sites, ROC curves were calculated. ROC analysis of BMD showed a best performance for DXA at the femoral neck (AUC: 0.670), followed by DXL at the calcaneus (AUC: 0.665), and DXA at the total hip (AUC: 0.661). Compared with these tests, DXA of lumbar spine had the lowest sensitivity according to ROC (AUC: 0.598). The difference between DXA of the lumbar spine and DXL at the calcaneus was statistically significant (p = 0.04; Figures 2, 3A).
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