TITLE: Portable Bone Mineral Density Scanners: A Review of the Clinical Effectiveness

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CONTEXT AND POLICY ISSUES:

Dual energy x-ray absorptiometry (DXA), which measures hip and spine bone mineral density (BMD), is the radiological densitometry currently accepted as an indicator of bone strength and fracture risk, and is the gold standard for BMD testing.\(^1\)\(^2\) DXA involves positioning the body site of interest in the path of an x-ray beam and measuring beam attenuation, which is related to bone mineral content.\(^2\) The World Health Organization (WHO) has established criteria for classification of normal, osteopenic, and osteoporotic based on bone density scores at any skeletal site in white women.\(^3\)

BMD scores obtained from different skeletal sites cannot be directly compared; instead a T-score for BMD is given in terms of standard deviation (SD) above or below the average value for “young normal” adults.\(^3\) A T-score greater than -1 is considered normal, T-score between -1 and -2.5 is osteopenia, and a T-score below -2.5 indicates osteoporosis.\(^4\) When BMD decreases from “young normal” levels, the risk of fracture increases.\(^3\) BMD values can also be expressed as Z-scores, which are also expressed in terms of SD. Z-scores are not used for evaluating patient’s risk of fracture, but are useful in comparing the patient with someone of the same age.\(^3\)

Portable bone density scanners include peripheral DXA and quantitative ultrasound devices, which are at modest cost, portable, can be operated in a variety of clinical settings, and provide useful information in assessing fracture risk.\(^5\)^{\textit{6}} Peripheral DXA measurements are performed at the wrist or heel.\(^6\) Compared to central DXA, peripheral DXA is associated with very low radiation doses. The ability of peripheral DXA to predict fracture risk of spine and hip may be weaker than that of central DXA.\(^8\)

Ultrasound devices measure different sites including the heel, patella, and finger.\(^7\) The ultrasound assessment involves placing ultrasound transducers on either side of the heel; one acts as a wave transducer, and the other acts as the receiver.\(^8\) Three main types of parameters
being assessed include broadband ultrasound attenuation, speed of sound, and quantitative ultrasound index stiffness. The quantitative ultrasound can predict future fracture risk as well as DXA, and may be able to assess bone quality in addition to BMD. It does not involve ionizing radiation, and does not require special trained personnel.

This report reviews the effectiveness of portable BMD scanners, and the evidence for their use in colder climates.

RESEARCH QUESTIONS:

1. What is the clinical effectiveness of portable bone mineral density (BMD) scanners for screening and diagnosis of osteoporosis compared to standard BMD scanners?

2. Should two sites (i.e: wrist and ankle) be scanned by portable BMD scanners for effective diagnosis of osteoporosis?

3. What is the evidence for the clinical effectiveness of portable BMD scanners in cold climates?

METHODS:

A limited literature search was conducted on key health technology assessment resources, including PubMed, The Cochrane Library (Issue 4, 2008), University of York Centre for Reviews and Dissemination (CRD) databases, ECRI, EuroScan, international health technology agencies, and a focused Internet search. Results include articles published between 2003 and January, 2009, and are limited to English language publications only. Filters were applied to limit the retrieval to certain study types: systematic reviews, health technology assessments, meta-analyses, guidelines, randomized controlled trials, and observational studies. Observational studies conducted in cold climate regions were included in the report.

SUMMARY OF FINDINGS:

One meta-analysis, two observational studies, and three guidelines were identified.

Clinical effectiveness

For quantitative ultrasound (QUS), one meta-analysis about the use of portable BMD for diagnosis of osteoporosis was identified.

The meta-analysis by Nayak et al. (2006) determined the sensitivity and specificity of calcaneal (heel) QUS for identifying patients who meet the WHO’s diagnostic criteria for osteoporosis. A systematic review was conducted and 25 studies where the analysis on the quantitative ultrasound index parameter was focused were included. Nine studies that presented threshold information (T-score units) were included in the regression analysis, where sensitivity and specificity were plotted against T-score threshold. The receiver-operating characteristic (ROC) curve of sensitivity (true positive rate) versus 1 – specificity (false positive rate) was also plotted. Limitations of this review include a small number of included studies and heterogeneity among studies.
Table 1: Analysis results for the QUS index parameter in Nayak et al.\(^8\)

<table>
<thead>
<tr>
<th>QUS T-score threshold</th>
<th>Sensitivity (95% CI)</th>
<th>Specificity (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.0</td>
<td>93 (87 – 97)</td>
<td>24 (10 – 47)</td>
</tr>
<tr>
<td>-0.5</td>
<td>88 (80 – 93)</td>
<td>39 (23 – 59)</td>
</tr>
<tr>
<td>-1.0</td>
<td>79 (69 – 86)</td>
<td>58 (44 – 70)</td>
</tr>
<tr>
<td>-1.5</td>
<td>66 (53 – 77)</td>
<td>74 (66 – 81)</td>
</tr>
<tr>
<td>-2.0</td>
<td>49 (33 – 66)</td>
<td>86 (80 – 90)</td>
</tr>
<tr>
<td>-2.5</td>
<td>33 (17 – 55)</td>
<td>93 (87 – 96)</td>
</tr>
</tbody>
</table>

The T-score thresholds of -0.5, -1.0, and -1.5 are clinically relevant because calcaneal QUS has higher sensitivity at these thresholds than it does at thresholds of less than -1.5.

Table 2 shows estimated post-test probability of DXA-determined osteoporosis at the hip or spine in women after testing with QUS index parameter.

Table 2: Post-test probability of DXA-determined osteoporosis at the hip or spine

<table>
<thead>
<tr>
<th>Age, y</th>
<th>Pre-test (%)</th>
<th>Estimated post-test probability of DXA-determined osteoporosis (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Threshold of -0.5: + result</td>
</tr>
<tr>
<td>50-59</td>
<td>15</td>
<td>20</td>
</tr>
<tr>
<td>60-69</td>
<td>22</td>
<td>28</td>
</tr>
<tr>
<td>70-79</td>
<td>39</td>
<td>47</td>
</tr>
<tr>
<td>&gt;80</td>
<td>70</td>
<td>77</td>
</tr>
</tbody>
</table>

The authors concluded that:

“The current available literature suggests that results of calcaneal QUS at commonly used cutoff thresholds do not definitely exclude or confirm DXA-determined osteoporosis. Additional research is needed before use of this test can be recommended in evidence-based screening programs for osteoporosis”.(page 832)\(^8\)

For portable dual energy x-ray absorptiometry (pDXA), two observational studies\(^9,10\) on the use of pDXA in colder climates were identified.

Andersen et al. (2005)\(^9\) conducted a cohort study to validate pDXA in rural Arctic Greenland, to measure the BMD in Greenland Inuit and Caucasians, and to estimate the importance of ethnicity for BMD. The BMD in 80 healthy subjects (Inuit/Caucasians, n=52/28; men/women, n=37/43; age: 30-49) living in Ilulissat and Saqqaq in North Greenland was measured twice in both distal forearms and in both heels using pDXA. Caucasians were bigger than Inuit, but had similar BMD.

Measurement of BMD did not differ with time or between sites for heel or distal forearm. The imprecision was within 2% for all calibration. Triplicate measurements in 11 subjects showed individual percent of coefficient of variation (CV%) from 0.16% to 1.79% in distal forearm and 0.38% to 1.53% in heel. The overall CV% in distal forearm and heel were 1.09% and 1.01%, respectively. Table 3 shows mean BMD in different investigation sites of men and women of Inuit and Caucasians.
Table 3: Mean BMD in different investigation sites

<table>
<thead>
<tr>
<th>Ethnicity/gender</th>
<th>Mean BMD (g/cm²)</th>
<th>Right forearm</th>
<th>Left forearm</th>
<th>Right heel</th>
<th>Left heel</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inuit</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Men</td>
<td>0.570</td>
<td>0.568</td>
<td>0.549</td>
<td>0.536</td>
<td></td>
</tr>
<tr>
<td>• Women</td>
<td>0.484</td>
<td>0.474</td>
<td>0.473</td>
<td>0.464</td>
<td></td>
</tr>
<tr>
<td>Caucasians</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Men</td>
<td>0.580</td>
<td>0.570</td>
<td>0.646</td>
<td>0.638</td>
<td></td>
</tr>
<tr>
<td>• Women</td>
<td>0.495</td>
<td>0.496</td>
<td>0.552</td>
<td>0.553</td>
<td></td>
</tr>
</tbody>
</table>

BMD of right and left limbs were identical between groups. Distal forearm BMD did not differ between Inuit and Caucasians (men/women, p=0.79/0.43) whereas heel BMD did (men/women, p=0.004/0.011). Ethnicity difference in heel BMD (p<0.001) disappeared when adjusted for weight (p=0.30). There were no differences in forearm BMD between Inuit and Caucasians.

The authors concluded that “pDXA is feasible and reliable in rural Greenland. Ethnic differences in BMD are small and may reflect differences in body size”.

Andersen et al. (2003) conducted a feasibility study to validate DXA scanning for use in the field studies in the Arctic region and to obtain data on BMD in Greenland Inuit. BMD was measured in 52 healthy Inuit (age 30-49) living in Ilulissat and Saqqaq in North Greenland using a portable DXA scanner. The measurement sites were both forearms and calcaneal bones. The results showed that imprecision was kept at 2% for all calibrations. The overall CV was 1.09% (0.16% – 1.79%) in the forearm and 1.01% (0.38% – 1.53%) in the heel. Mean BMD in men was 0.569 g/cm² in forearm and 0.542 g/cm² in the heel. Mean BMD in women was 0.479 g/cm² in the forearm and 0.468 g/cm² in the heel. The authors concluded that “DXA scanning is feasible, reliable and comfortable method in rural Greenland”.

Guidelines

Three guidelines on the use of portable BMD were identified, two on quantitative ultrasound and one on peripheral DXA.

The American College of Radiology (ACR) Appropriateness Criteria panel (2007) used broad-based consensus techniques and developed recommendations on osteoporosis and bone mineral density measurement. Recommendations relating to portable BMD scanners [i.e., the peripheral quantitative ultrasound (QUS)] were as follows:

“QUS should be used only in screening appropriate patients-postmenopausal and elderly who have not had a DXA and are unable to reach a DXA scanner easily because of rural location. This technology is used most frequently in health fairs or other screening events, and if a patient is identified as having an increased risk of fracture he or she should be referred for DXA to confirm the risk of fracture and provide a diagnosis. The DXA then establishes a baseline and follow-up can be performed. QUS can have false negatives and positives depending on the technology and its age. If a patient has multiple risk factors for fracture or low BMD he or she should be referred for DXA evaluation even if QUS is within normal limits. The use of QUS should be extremely limited with the number of DXA scanners available”.(page 9)

The International Society for Clinical Densitometry (ISCD) 2007 Position Development Conference addressed clinical applications of quantitative ultrasound (QUS) for fracture risk assessment, diagnosis of osteoporosis, treatment initiation, monitoring of treatment, and quality assurance/quality control. The ISCD QUS Task Force reviewed the medical literature and proposed a set of operational recommendations for the clinical use of QUS.
The recommendations were graded in four categories: Quality of evidence (Good, Fair, Poor); Strength of recommendation (A, B or C); Applicability (worldwide = W or variable, according to local requirements = L); and Necessity (necessary).

Technology diversity among QUS devices
- For QUS, bone density measurement from different devices cannot be directly compared. Grade: Good – A – W – Necessary(page 164)12

Can QUS be used for fracture risk assessment?
- The only validated skeletal site for the clinical use of QUS in osteoporosis management is the heel. Grade: Good – A – W – Necessary
- Validated heel QUS devices predict fragility fracture in postmenopausal women (hip, vertebral and global fracture risk) and men over the age of 65 (hip and all non-vertebral fractures), independently of central DXA BMD. Grade: Good – A – W – Necessary
- Discordant results between heel QUS and central DXA are not infrequent and are not necessarily an indication of methodological error. Grade: Good – A – W – Necessary
- For QUS, different devices should be independently validated for fracture risk prediction by prospective trials or by demonstration of equivalence to a clinically validated device. Grade: Good – B – W – Necessary(page 165)

Can QUS be used to diagnose osteoporosis?
- The WHO diagnostic classification cannot be applied to T-scores from measurements other than DXA at the femur neck, total femur, lumbar spine or one-third (33%) radius because those T-scores are not equivalent to T-scores derived by DXA. Grade: Good – A – W – Necessary(page 167)

Can QUS be used to initiate treatment?
- Central DXA measurements at the spine and femur are the preferred method for making therapeutic decisions and should be used if possible. However, if central DXA cannot be done, pharmacologic treatment can be initiated if the fracture probability, as assessed by heel QUS using device specific thresholds and in conjunction with clinical risk factors, is sufficiently high. Grade: Fair – C – W – Necessary
- Heel QUS in conjunction with clinical risk factors can be used to identify a population at very low fracture probability in which no further diagnostic evaluation may be necessary. Grade: Good – B – W – Necessary(page 169)

Can QUS be used to monitor treatment?
- QUS cannot be used to monitor the skeletal effects of treatments for osteoporosis. Grade: Good – A – W – Necessary(page 175)

What are the quality assurance and quality control criteria for QUS?
- For QUS, device-specific education and training should be given to the operators and interpreters prior to clinical use. Grade: Good – A – W – Necessary
- Quality control procedures should be performed regularly. Grade: Good – A – W – Necessary (page 177)12

The ISCD 2007 Position Development Conference addressed clinical applications of peripheral dual-energy X-ray absorptiometry (pDXA) for fracture risk assessment, diagnosis of osteoporosis, treatment initiation, monitoring of treatment, and quality assurance/quality control.13 The ISCD pDXA Task Force reviewed the medical literature and proposed a set of operational recommendations for the clinical use of pDXA.
The recommendations were graded in four categories: Quality of evidence (Good, Fair, Poor); Strength of recommendation (A, B or C); Applicability (worldwide = W or variable, according to local requirements = L); and Necessity (necessary)

Technology diversity among pDXA devices
- For pDXA, bone density measurement from different devices cannot be directly compared. Grade: Good – A – W – Necessary

Can pDXA be used for fracture risk assessment?
- Measurement by validated pDXA devices can be used to assess vertebral and global fragility fracture risk in postmenopausal women, however its vertebral fracture predictive ability is weaker than central DXA and heel QUS. There is a lack of sufficient evidence to support this position for men. Grade: Fair – B – W – Necessary
- For pDXA, different devices should be independently validated for fracture risk prediction by prospective trials or by demonstration of equivalence to a clinically validated device. Grade: Good – B – W – Necessary

Can pDXA be used to diagnose osteoporosis?
- The WHO diagnostic classification can only be applied to DXA at the femur neck, total femur, lumbar spine or one-third (33%) radius region of interest measured by DXA or pDXA devices utilizing a validated young-adult reference database. Grade: Good – A – W – Necessary

Can pDXA be used to initiate treatment?
- Central DXA measurements at the spine and femur are the preferred method for making therapeutic decisions and should be used if possible. However, if central DXA cannot be done, pharmacologic treatment can be initiated if the fracture probability, as assessed by radius pDXA (or DXA) using device specific thresholds and in conjunction with clinical risk factors, is sufficiently high. Grade: Fair – B – W – Necessary
- Radius pDXA in conjunction with clinical risk factors can be used to identify a population at very low fracture probability in which no further diagnostic evaluation may be necessary. Grade: Fair – B – W – Necessary

Can pDXA be used to monitor treatment?
- pDXA devices are not clinically useful in monitoring the skeletal effects of presently available medical treatment for osteoporosis. Grade: Good – A – W – Necessary

What are the quality assurance and quality control criteria for pDXA?
- For pDXA, device-specific education and training should be given to the operators and interpreters prior to clinical use. Grade: Good – A – W – Necessary
- Quality control procedures should be performed regularly. Grade: Good – A – W – Necessary

Limitations
Limited information was identified on portable BMD scanners and therefore interpretation should be done with caution. No studies comparing portable BMD scanners with standard BMD scanners were identified. Although there are two comprehensive ISCD guidelines on the use of QUS and peripheral DXA in BMD measurement, limited studies and systematic reviews were identified in this review. It is difficult to address the research questions with the limited information from the included studies.
CONCLUSIONS AND IMPLICATIONS FOR DECISION OR POLICY MAKING:

Two types of portable BMD scanners identified in this review are QUS and peripheral DXA. The heel is the validated site for QUS, while wrist or heel measurements are used for peripheral DXA. QUS appears to be better than peripheral DXA in the fracture risk assessment, according to the ISCD guidelines. These guidelines indicated that BMD measurements of different devices could not be directly compared. Each device should be well-calibrated and have its T-score thresholds established and validated. Both heel QUS and peripheral DXA should not be used to diagnose osteoporosis based on the WHO criteria. If central DXA is not available, heel QUS or peripheral DXA could be used in conjunction with clinical risk factors to initiate treatment or for screening of populations with low fracture risk. The guidelines also suggested that portable BMD scanners should not be used to monitor treatment since their performance could be affected by day-to-day variability. Evidence from two observational studies showed that peripheral DXA is feasible to operate in cold climates. No information was identified on the number of sites that should be scanned with portable BMD scanners. The limited information should be considered when deciding about the use of portable BMD scanners.

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