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Diagnostic Performance and Cost-Effectiveness of Technologies to Measure Bone Mineral Density in Postmenopausal Women

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CADTH
600-865 Carling Avenue
Ottawa ON Canada K1S 5S8
Tel. (613) 226-2553
Fax. (613) 226-5392
E-mail: pubs@cadth.ca

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Canadian Agency for Drugs and Technologies in Health

Diagnostic Performance and Cost-Effectiveness of Technologies to Measure Bone Mineral Density in Postmenopausal Women

Lesley Dunfield, PhD[1]
Monika Mierzwinski-Urban, MLIS[1]
Amanda Hodgson, MLIS[1]
Ray Banks, MLIS[1]

December 2007

[1] Canadian Agency for Drugs and Technologies in Health

Health technology assessment (HTA) agencies face the challenge of providing quality assessments of medical technologies in a timely manner to support decision making. Ideally, all important deliberations would be supported by comprehensive health technology assessment reports, but the urgency of some decisions often requires a more immediate response.

The Health Technology Inquiry Service (HTIS) provides Canadian health care decision makers with health technology assessment information, based on the best available evidence, in a quick and efficient manner. Inquiries related to the assessment of health care technologies (drugs, devices, diagnostic tests, and surgical procedures) are accepted by the service. Information provided by the HTIS is tailored to meet the needs of decision makers, taking into account the urgency, importance, and potential impact of the request.

Consultations with the requestor of this HTIS assessment indicated that a review of the literature would be beneficial. The research question and selection criteria were developed in consultation with the requestor. The literature search was carried out by an information specialist using a standardized search strategy. The review of evidence was conducted by one internal HTIS reviewer. The draft report was internally reviewed and externally peer-reviewed by two or more peer reviewers. All comments were reviewed internally to ensure that they were addressed appropriately.

Reviewers

CADTH takes sole responsibility for the final form and content of this bulletin. The statements and conclusions in this bulletin are those of CADTH and not of the reviewers.

Reviewer who agreed to be acknowledged:

Sophie A. Jamal, MD PhD FRCPC
Endocrinologist, Assistant Professor of Medicine
University of Toronto
Toronto ON

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Date: October 15, 2007

1 EXECUTIVE SUMMARY

Context and policy issues

Osteoporosis is a progressive disease characterized by low bone mass, microarchitectural bone tissue deterioration and loss of bone strength that can lead to an increased risk of fracture. The World Health Organization's (WHO) definition of osteoporosis is a T score of ≤ -2.5, which is equivalent to a hip bone mineral density (BMD) of greater than or equal to 2.5 standard deviations below the young adult female reference mean. Osteoporosis is common in postmenopausal women, and 80% of the approximately one million Canadians with osteoporosis are women.

Different techniques are available to measure BMD. The gold standard for measuring BMD to diagnose osteoporosis is central dual-energy x-ray absorptiometry of the hip (DXA, DEXA). Quantitative ultrasonography (QUS), quantitative computed tomography (QCT), and radiographic absorptiometry can also be used.

The effectiveness of the technologies to assess BMD to diagnose osteoporosis is examined in this report. Because of the limited availability and the cost implications of central DXA devices, an assessment of the effectiveness of alternative devices is required to determine their usefulness for predicting fracture risk in postmenopausal women.

Research Questions

1. What is the diagnostic performance of the technologies used to measure BMD (i.e., peripheral densitometry, quantitative computed tomography, quantitative ultrasonography, radiography absorptiometry) compared to dual-energy x-ray absorptiometry when used to evaluate the risk of osteoporotic fracture in postmenopausal women?
2. What are the comparative economic considerations relative to the use of the different technologies to measure BMD?

Methods

Published literature was identified by cross-searching Biosis, Embase, and Medline databases on the OVID search system. Parallel searches were performed on the Cochrane Library (Issue 2, 2007) databases. Retrieval was limited by human population, English or French language, and publications from 2002 to September 13, 2007. RCTs were limited to publications from 2005 to September 13, 2007. Some manual searches of relevant articles were conducted. Filters were applied to limit the retrieval to systematic reviews, RCTs, and economic studies.

One reviewer selected articles and extracted data. Studies were included that compared at least two methods of measuring BMD in postmenopausal women. Studies were excluded if they were not peer-reviewed or were not full publications.

Findings

Two systematic reviews, six observational studies, and three studies on economic considerations were included in this report.

Comparative clinical effectiveness
A Canadian systematic review concluded that predicting fracture risk in postmenopausal women was best done using DXA but that QUS was comparable to DXA for the measurement of BMD. Limited information was available from the other systematic review because of language restrictions. The authors concluded that there was uncertainty regarding the comparisons of DXA, QUS, and QCT. The observational studies varied in the methods used to discriminate fractures. The power of a diagnostic test can be expressed as area under the curve (AUC) computed from the receiver operator characteristic (ROC) curve. An AUC close to

1.0 indicates a perfect test, and an AUC close to 0.5 indicates a test of little value. One study comparing DXA to QUS found an AUC of 0.59 to 0.63 for BMD by DXA and 0.62 for QUS. Two other studies found AUCs of 0.86 to 0.95 for DXA and 0.93 for QUS and 0.60 to 0.66 for DXA and 0.60 for QUS. DXA, QUS, and QCT were compared in one study, which found AUCs of 0.843 to 0.896 for DXA, 0.876 for QCT, and 0.604 to 0.869 for QUS. DXA and QCT were compared in one study, which found AUC to be 0.647 for DXA and 0.870 for QCT. There were no differences in odds ratios (ORs) that were reported in some studies, with one exception in which the OR for BMD determined by using DXA was 4.8, and that determined using QCT (MDCT) was 12.7.

Cost-effectiveness

Three studies reported on costs for technologies to measure BMD. A study from Thailand reported the cost-effectiveness ratio in US dollars to be US$88.42 per fracture prevented for DXA and US$146.48 per fracture prevented for QUS. A US study found DXA cost US$703,000 per 1,000 women to prevent 7.8 hip fractures, QUS cost US$632,000 per 1,000 women to prevent 6.7 hip fractures, and sequentially testing by QUS then DXA cost US$442,000 per 1,000 women to prevent 5.7 fractures. A Spanish study found that the total cost per correctly detected case of osteoporosis was €23.85 for DXA and €22.00 for QUS.

Conclusions and implications for policy making
The AUC for DXA ranged from 0.59 to 0.95 for the different bones analyzed in the different studies. QUS AUC ranged from 0.60 to 0.93, and QCT AUC ranged from 0.87 to 0.93 in the studies. There do not seem to be major differences between DXA and QUS in the studies. ORs for discriminating fractures were reported for four of the six studies and ranged from 1.35 to 4.8 for DXA, 1.26 to 4.18 for QUS, and 12.7 to 16 for QCT. There were no major differences between the ORs in the studies, except in the study on MDCT and DXA where the OR was higher for MDCT compared to DXA. The costs for DXA and QUS were similar in two cost studies. It is unknown, however, whether any of these studies could be translatable to a Canadian setting.

QCT seems to be at least as effective as DXA. QCT, however, uses more radiation than DXA. Overall, QUS seems to be comparable to DXA for discriminating fractures in postmenopausal women, although this is based on low quality evidence. Other factors such as the lack of radiation used for QUS and the limited availability of DXA may help to determine which screening test would be most useful. None of these were Canadian studies and more research is needed on the methods to measure BMD in postmenopausal women.

2 CONTEXT AND POLICY ISSUES

Osteoporosis is a progressive disease characterized by low bone mass, microarchitectural bone tissue deterioration, and loss of bone strength that can lead to an increased risk of fracture.[1-3] Osteoporosis is common in postmenopausal women, and 80% of the approximately one million Canadians with osteoporosis are women.[1,4] Women with low body mass, weight loss, family history of osteoporosis, lack of physical activity, consumption of alcohol, and low intake of vitamin D are at increased risk of osteoporosis and osteoporotic fractures.[1] Consumption of caffeine and low intake of calcium may also increase the risk of osteoporosis.[1,3]

The World Health Organization's (WHO) definition of osteoporosis is a T score of ≤ -2.5, which is equivalent to a hip bone mineral density (BMD) of greater than 2.5 standard deviations below the young adult female reference mean.[2,3,5] Different technologies are available to measure BMD. The gold standard for measuring BMD to diagnose osteoporosis is central dual-energy x-ray absorptiometry (DXA; DEXA).[2] BMD of the hip is the most accurate method to predict fracture risk.[1] DXA is a non-invasive measurement that produces accurate and reproducible results to predict fracture risk.[2] The portable DXA devices that measure BMD at the wrist, heel, or finger may not be as precise as

central DXA and are most useful for predicting fracture risk, but not for diagnosing osteoporosis.[1,2] The main disadvantages to DXA in addition to the use of radiation are the limited accessibility, because the devices are not portable, and the expense.[1,3]

Quantitative ultrasonography (QUS) can be used to predict fracture risk by measuring sound transmission through the patella or calcaneus. The results are related to BMD and skeletal strength.[1] QUS does not use ionizing radiation, which is its advantage over DXA.[1,6,7] Another advantage is the accessibility.[1] QUS devices are portable, as opposed to DXA devices, which are mainly confined to clinics and are of limited availability.[1,7,8] QUS has been reported to be less costly than DXA.[1,7,9] In addition, QUS can be used to assess the structural aspects of bone, such as microarchitectural competence, which may contribute to bone strength.[10]

Quantitative computed tomography (QCT) can be used to measure BMD. It uses a higher dose of radiation than DXA, it can be more costly, and its results are less reproducible.[1] Multi-detector row CT is a type of QCT that has a higher spatial resolution compared with that of standard spiral CT.[11] Radiographic absorptiometry is an inexpensive technique that involves imaging the phalanges using an x-ray machine and comparing the density to that of a standardized aluminum wedge.[1]

The power of a diagnostic test can be expressed as area under the curve (AUC) computed from the receiver operator characteristic (ROC) curve. An AUC close to 1.0 indicates a perfect test, and an AUC close to 0.5 indicates a test of little value.[12] The effectiveness of the technologies used to assess BMD to diagnose osteoporosis is examined in this report. Because of the limited availability and the cost implications of DXA devices, an assessment of the effectiveness of alternative devices is needed to determine their usefulness for predicting the fracture risk in postmenopausal women.

3 RESEARCH QUESTIONS

1. What is the diagnostic performance of the technologies used to measure BMD (i.e., peripheral densitometry, quantitative computed tomography, quantitative ultrasonography, radiography absorptiometry) compared with dual-energy x-ray absorptiometry when used to evaluate the risk of osteoporotic fracture in postmenopausal women?
2. What are the comparative economic considerations related to the use of different technologies to measure BMD?

4 METHODS

Published literature was obtained by cross-searching BIOSIS, EMBASE, and MEDLINE databases on the OVID search system. Parallel searches were performed on the Cochrane Library (Issue 2, 2007) databases. Regular alerts were established on BIOSIS, EMBASE, and MEDLINE, and information retrieved via alerts is current to September 13, 2007. Retrieval was limited by human population, English or French language, and publications from 2002 to September 13, 2007. RCTs were limited to publications from 2005 to September 13, 2007. Filters were applied to limit the retrieval to systematic reviews, RCTs, and economic studies.

The web sites of regulatory agencies and health technology assessment and related agencies were searched as were specialized databases such as those of the University of York Centre for Reviews and Dissemination. Also, some manual searches of relevant articles were conducted. The Google search engine was used to search for information on the Internet.

One reviewer selected articles and extracted data. The eligibility criteria were established a priori. Studies were included if they compared at least two methods of measuring BMD in postmenopausal women. Studies were excluded if they were not peer-reviewed (conference reports) or if they were not full publications (abstracts).

5 FINDINGS

Articles were selected if they described the use of DXA and at least one other method in the measurement of BMD in postmenopausal women. Two systematic reviews, six observational studies, and three studies on economic considerations were included in this report. Table 1 summarizes the data from the observational studies. The systematic reviews were published in 2002 and 2003. Therefore, the studies included in those reviews do not overlap with the studies included in this report because of the date limitations.

5.1 Comparative Clinical Effectiveness

The Osteoporosis Society of Canada has conducted a systematic review of the literature on the diagnosis and management of osteoporosis.[3] Two reviewers retrieved abstracts, and at least two reviewers independently reviewed the literature. Four levels of evidence were used to grade the evidence:

- level 1 – test results and the diagnostic standard were independently interpreted, patients not known to have the disorder but suspected to have the disorder were selected, the test and the diagnostic standard were reproducibly described, and there were at least 50 people in each group
- level 2 – four of the criteria for level 1 met
- level 3 – three of the criteria for level 1 met
- level 4 – one or two of the criteria for level 1 met.

Level 1 evidence showed that predicting fracture risk in postmenopausal women was best done using DXA. Level 1 evidence showed that QUS was comparable to DXA in measuring BMD to estimate fracture risk. Consensus evidence suggests that radiogrammetry, radiographic absorptiometry, and QUS may be useful when DXA is unavailable because of geography and limited access.

The Swedish Council on Technology Assessment in Health Care has published a systematic review on the prevention, diagnosis, and treatment of osteoporosis.[5] Only the summary and conclusions of this systematic review were available in English; the full article is available in Swedish. The report compared DXA, quantitative computed tomography (QCT), and quantitative ultrasound (QUS) for diagnosing osteoporosis. The precision of the tests was found to be 0.5% to 3% for DXA, 1.5% to 6% for QUS, and 2% to 6% for QCT. The accuracy was 3% to 9% for DXA and 5% to 15% for QCT (not reported for QUS). The relative risk of fracture in postmenopausal women with a T score of −1 was 1.5 for DXA and QUS. Because of the limited information in the summary of this systematic review, it is difficult to determine how comparisons were made between the technologies. The authors concluded that there is uncertainty regarding the comparisons of DXA, QUS, and QCT.

A prospective study was conducted to compare DXA and QUS for fracture risk in postmenopausal women.[13] Between 1990 and 1994, 5,119 women were selected for a DXA scan of the hip and lumbar spine. A QUS scan of the left heel was also conducted in 1,000 women who consented. During a second visit between 1997 and 2000, previous fractures were recorded, and another set of scans were performed. A total of 3,883 women (75.8%) completed the follow-up visit. Of these, 775 received the DXA and QUS scan. In the total population, the average age was 48.6 years, and the average weight was 66.2 kg. In the QUS subgroup, the average age was 47.8 years, the average height was 1.61 m, the average weight was 65.9 kg, and the average BMI was 25.3. There was no information about the personnel administering the scans and their level of training or experience. The ROC analysis of the total population found AUCs of 0.62 for spine BMD and 0.59 for femoral neck BMD, which were both significant to predict fractures (P <0.001). The ROC analysis for the subgroup that received QUS and DXA found an AUC of 0.63 for spine BMD, 0.59 for neck BMD, and 0.62 for QUS. The hazard ratios for osteoporotic fracture were 1.80 for spine BMD, 2.16 for femoral neck BMD, and 2.25 for QUS. Because the hazard ratio for QUS was higher than that for DXA, the authors suggested that QUS may be a better predictor of fractures than DXA.

QUS was compared with DXA in postmenopausal women without fractures (n=770) and with vertebral fractures (n=764) in a retrospective study to discriminate women with vertebral fracture from women without fracture.[7] The average age was 71.8 years in the subjects without fracture and 73.6 years in the subjects with fracture. In subjects without fracture and in those with fracture, the average weight was 65.3 kg and 56.77 kg. DXA of the total body, lumbar spine, total femur, and femoral neck and QUS of the left heel were done. The QUS measurements were reported as stiffness. Speed of sound (SOS) and broadband ultrasound attenuation (BUA) are measures of QUS that are used to calculate the stiffness index. The risk of fracture can be determined from the stiffness index. Stiffness correlations were 0.66 with total body BMD, 0.62 with lumbar spine BMD, and about 0.5 with femoral BMD (P <0.01). The age-adjusted odds ratios (OR) after correction for years of menopause, weight, height, and BMI were not significantly different. The ORs for discriminating fractures were 4.18 for stiffness, 3.95 for total body BMD, 4.18 for lumbar spine BMD, 3.07 for total femur BMD, and 3.13 for femoral neck BMD, which were all significant for discriminating fractures (P value not reported). The AUC from the ROC analysis were 0.94 for total body, 0.95 for lumbar spine, 0.86 for total femur, 0.89 for femoral neck, and 0.93 for QUS. The sensitivities and specificities were also reported. The sensitivities were 89.3% for total body, 98.7% for lumbar spine, 72.5% for total femur, 73.1% for femoral neck, and 93.8% for stiffness. The specificities were 81.6% for total body, 71.3% for lumbar spine, 67.1% for total femur, 72.2% for femoral neck, and 69.6% for stiffness. Overall, this study found that QUS is a good tool for assessing the risk of vertebral fracture in postmenopausal women, because the results are comparable to those of DXA, QUS does not use x-rays, and the authors report it to be less costly. A possible limitation to this study is that it is unclear whether testing by DXA and QUS was done on the same day, because testing on different days may affect results. In addition, there was no information about the personnel administering the test.

A study was done to identify the thresholds for identifying women with osteoporosis using different peripheral devices.[9] DXA (lumbar spine, total hip, and distal forearm), QCT (distal forearm), and QUS (heel, finger, and radius and metatarsal) were done in 500 postmenopausal women. All tests were done in all subjects on the same day by trained radiographers and technicians. The average age was 67.4 years, and the average weight was 70.8 kg. The threshold above a 95% certainty that the patient does not have osteoporosis (95% sensitivity) and the threshold below a 95% certainty that the patient does have osteoporosis (95% specificity) were determined. The QUS devices measured broadband ultrasound attenuation (BUA) and speed of sound (SOS). Compared with the total hip BMD as measured by DXA, there was a significant difference in the AUC of the different devices and sites (P <0.0001). The AUC was 0.896 for forearm DXA, 0.843 for spinal DXA, and 0.876 for forearm QCT and ranged from 0.604 to 0.800 for SOS and from 0.848 to 0.869 for BUA. There was a difference in specificities between the different devices at 95% sensitivity. The specificity was 28% for spinal DXA, 72% for forearm DXA, 62% for QCT, 40% to 55% for BUA, and 27% to 44% for SOS. The sensitivities at 95% specificity were 41% for spinal DXA, 32% for forearm DXA, 41% for QCT, 22% to 39% for BUA, and 17% to 29% for SOS. The threshold approach identified 68% of subjects with a 95% sensitivity and specificity.

DXA of the lumbar spine and QCT of the spine was used to measure BMD in 82 postmenopausal women with (n=39) or without fracture (n=43).[11] The average age was 64.4 years for the women without fracture and 66.2 years for the women with fracture. The weight was 52.8 kg and 50.1 kg for women without fracture or with fractures respectively. QCT was done using multi-detector row CT (MDCT). In addition to measuring BMD, MDCT scanning measured microstructure parameters such as structure model index (SMI), bone volume/total volume (BV/TV), and trabecular number and thickness. The AUC values for BMD and SMI were calculated from the ROC analysis. The AUC was significantly higher for SMI (0.928)

compared with BMD by DXA (0.647) and BMD by MDCT (0.870). The AUCs for other microstructure parameters ranged from 0.629 to 0.857. ORs for predicting fracture were lower for DXA BMD (OR=4.8) than SMI (OR=16) and BMD by MDCT (OR=12.7). ORs ranged from 3.5 to 13.6 for the other microstructural parameters. The authors concluded that MDCT may be better for predicting fracture risk than DXA. Possible limitations to this study include the small sample size, the lack of information about the personnel conducting the scans, and the fact that it is unclear whether testing using the different methods was done on the same day.

Table 1: AUC, ORs, and sensitivity and specificity of technologies to measure BMD

Study	Patient Number	Test	AUC	OR (95% CI)	Sensitivity	Specificity
Stewart *et al.*[13]	775	spine DXA	0.63 (0.60 to 0.67)*	HR = 1.80 (1.17 to 2.77)*	NR	NR
		femoral neck DXA	0.59 (0.56 to 0.63)*	HR = 2.16 (1.35 to 3.47)	NR	NR
		QUS	0.62 (0.59 to 0.66)*	HR = 2.25 (1.51 to 3.34)	NR	NR
Frediani *et al.*[7]	1,534	total body DXA	0.94 (0.4)†	3.95 (3.08 to 6.16)	89.3%	81.6%
		spinal DXA	0.95 (0.3)†	4.18 (3.05 to 6.82)	98.7%	71.3%
		femoral DXA	0.86 (0.6)†	3.07 (2.84 to 7.81)	72.5%	67.1%
		femoral neck DXA	0.89 (0.3)†	3.13 (2.76 to 6.90)	73.1%	72.2%
		QUS	0.93 (0.4)†	4.18 (3.35 to 7.13)	93.8%	69.6%
Clowes *et al.*[9]	500	spinal DXA	0.843 (0.808 to 0.874)*	NR	41%	38%
		forearm DXA	0.896 (0.865 to 0.921)*	NR	32%	72%
		QCT	0.876 (0.839 to 0.908)*	NR	41%	62%
		BUA by QUS	0.848 (0.813 to 0.879) to 0.869 (0.832 to 0.898)*	NR	22% to 39%	40% to 55%
		SOS by QUS	0.604 (0.558 to 0.648) to 0.800 (0.762 to 0.834)*	NR	17% to 29%	27% to 44%
Ito *et al.*[11]	82	SMI by MDCT	0.928 ± 0.027†‡	16.0 (5.3 to 48.4)‡	NR	NR
		MDCT	0.870 ± 0.040†‡	12.7 (4.4 to 36.4)‡	NR	NR
		DXA	0.647 ± 0.062†	4.8 (1.5 to 14.8)	NR	NR
Glüer *et al.*[10]	87	DXA spine	NR	2.13 (1.08 to 4.16)	NR	NR
		DXA whole body	NR	2.37 (1.20 to 4.70)	NR	NR
		SOS by QUS	NR	2.58 (1.17 to 5.68)	NR	NR
		BUA by QUS	NR	2.13 (1.04 to 4.34)	NR	NR
		stiffness	NR	2.83 (1.26 to	NR	NR

Table 1: AUC, ORs, and sensitivity and specificity of technologies to measure BMD						
Study	**Patient Number**	**Test**	**AUC**	**OR (95% CI)**	**Sensitivity**	**Specificity**
				6.34)		
		radiology	NR	3.03 (1.69 to 5.26) to 3.85 (1.96 to 7.69)	NR	NR
Alexander sen *et al.*[6]	1,034	DXA total femur	0.66 ± 0.2 (0.62 to 0.71)*‡	1.85 (1.55 to 2.20)	NR	NR
		DXA femoral neck	0.66 ± 0.2 (0.62 to 0.71)*‡	1.81 (1.51 to 2.16)	NR	NR
		DXA distal radius	0.64 ± 0.2 (0.59 to 0.68)*‡	1.47 (1.28 to 1.68)	NR	NR
		DXA total body	0.63 ± 0.2 (0.58 to 0.67)*‡	1.57 (1.32 to 1.86)	NR	NR
		DXA lumbar spine	0.60 ± 0.2 (0.56 to 0.65)*‡	1.35 (1.19 to 1.54)	NR	NR
		SOS by QUS	0.60 ± 0.2 (0.56 to 0.65)*‡	1.26 (1.12 to 1.42)	NR	NR
		UBPI by QUS	0.60 ± 0.2 (0.55 to 0.64)*‡	1.55 (1.26 to 1.90)	NR	NR

*95% CI (confidence interval); †standard error; ‡statistically significant. AUC=area under curve; BUA=broadband ultrasound attenuation; DXA=dual energy x-ray absorptiometry; HR=hazard ratio; MDCT=multi-detector row CT; NR=not reported; OR=odds ratio; QCT=quantitative computed tomography; QUS=quantitative ultrasound; SMI=structure model index; SOS=speed of sound; UPBI=ultrasound bone profile index

Radiography, DXA, and QUS were assessed for predicting fracture risk in 124 postmenopausal women with osteoporosis.[10] Of these women, 67 had a vertebral fracture, and 57 had no fractures. The average age was 64.75 years for patients with no fractures and 66.12 years for patients with fractures. Women with BMD less than 0.825 g/cm^2 with osteoporosis were included in the study, and 83% of them were receiving treatment for osteoporosis at the baseline visit. DXA of the femur, lumbar spine, and whole body was done. SOS and BUA were measured using QUS, and the stiffness index was calculated. All whole body DXA scans were done by the same operator, and the other scans were conducted by three cross-trained operators. Of the initial 124, 87 attended the two-year follow-up. The ORs for prediction of fracture in the two-year subset for BMD were 2.13 for spine and 2.37 for whole body. The OR for SOS was 2.58, BUA was 2.13, and stiffness was 2.83. ORs for radiology ranged from 3.03 to 3.85. Overall, this study showed that radiographic measure can identify women with vertebral fracture. A possible limitation to this study is that all patients had osteoporosis, were currently undergoing treatment for osteoporosis, and had other health problems that may have had an effect on the results of this testing. In addition, a small sample size was used in this study.

A comparison of DXA and QUS was done to identify fractures in a study of 1,034 postmenopausal women.[6] Women were excluded if they were on medication that could influence calcium metabolism during the six months before the follow-up visit. The average age was 69.9 years, and the average weight was 67.5 kg. BMD by DXA was measured at the lumbar spine, total hip, femoral neck, distal radius, and total body. QUS was done of the phalanges, and SOS and ultrasound bone profile index (UBPI) were analyzed.

The AUCs for determining fractured from non-fractured subjects were 0.60 to 0.66 for BMD of the various regions and 0.60 for both SOS and UBPI. The age- and BMI-adjusted ORs for BMD were 1.82 for total femur, 1.70 for femoral

neck, 1.36 for distal radius, 1.45 for total body, and 1.35 for lumbar spine. The OR was 1.20 for SOS and 1.39 for UBPI. The authors concluded that QUS may be used to identify patients with osteoporosis. This study did not state whether the testing by QUS and DXA were conducted on the same visit and did not state details about the technician who performed the scans. Women had previously been screened for osteoporosis at the research institute and therefore may not reflect the total population.

5.2 Cost-Effectiveness

The costs of DXA and QUS were compared in a study from Thailand.[14] The Thai baht was converted to 2004 US dollars in this study. Limited information was available about the cost-effectiveness analysis, and the perspective was not stated. A decision tree analysis was done on a hypothetical cohort of perimenopausal women. The cost-effectiveness ratio (CER) was found to be US$88.42 per fracture prevented for DXA and US$146.48 per fracture prevented for QUS. Therefore, the cost per fracture prevented was less for DXA than QUS. The incremental cost effectiveness ratio (ICER) for fracture prevention was US$79,930 for DXA and US$137,990 for QUS, calculated from the CER, the cost of no intervention, and the risk reduction. A sensitivity analysis suggested that changes in the costs of treating fractures and the prevalence of osteoporosis may affect these results.

A US economic comparison of QUS and DXA was conducted.[15] Using a decision-analytical model, a hypothetical cohort of 1,000 women was used to determine the costs of DXA and QUS for osteoporosis diagnosis. This study was limited in that QALYs were not used as the outcome. DXA was found to cost US$703,000 per 1,000 women to prevent 7.8 hip fractures (US $90,128 per 1,000 women per fracture prevented). QUS cost US$632,000 per 1,000 women to prevent 6.7 hip fractures (US $94,328 per 1,000 women per fracture prevented). A sequential approach of QUS followed by DXA cost US$442,000 per 1,000 women to prevent 5.7 fractures (US$77,544 per 1,000 women per fracture prevented). Therefore, this approach had the lowest cost.

A cost-effectiveness analysis from Spain was conducted to determine the costs of DXA compared with using QUS as a prescreening tool in 267 postmenopausal women.[16] A decision analytical model and the health services perspective were used. The cost for DXA was €13.31 per scan, compared with €1.66 for QUS. Two hundred and eight women were referred for DXA after QUS because of uncertain QUS results. The total cost was €3,554 for DXA and €3,211 for QUS plus DXA, calculated by multiplying the cost of each test with the number of women who had the test [DXA = 267 × 13.31; QUS+DXA = (267 × 1.66) + (208 × 13.31)]. The total cost per correctly detected case of osteoporosis was €23.85 for DXA ($3,554 / 149) and €22.00 for QUS ($3,211 / 146). The sensitivity analysis found that increasing the number of DXA scans performed per year reduced the costs. Overall, the costs for both methods were similar.

5.3 Limitations

Two systematic reviews were found, and one was not published in English, so the quality of this review could not be assessed. No randomized controlled trials (RCTs) that assessed the effectiveness of technologies to measure BMD for the detection of fracture risk in postmenopausal women were found. None of the included studies was Canadian. Six observational studies from 2005 to the present were included. These are, however, of lesser quality than RCTs, because observational studies do not control for potential bias. This report included only studies that compared at least two technologies; there were no studies that compared all the technologies of interest. One study[6] tested for inter-rater and intra-rater reliability. General limitations of the observational studies include the possibility that the outcomes of the tests could be influenced by the technician performing the tests, because differences in training and experience could affect the results. In addition, different devices (i.e., different manufacturers) were used in the studies and may contribute to the variation in the results. One study looked at radiology, and two looked at QCT; most studies compared QUS with DXA. The observational studies were

heterogeneous with respect to the patient population, the devices used, and the bones analyzed, which make comparisons of the technologies to assess BMD difficult. The economic studies were limited to three studies: one from the US, one from Spain, and one from Thailand. It is difficult to determine whether these studies would be translatable to a Canadian context.

6 CONCLUSIONS AND IMPLICATIONS FOR DECISION OR POLICY MAKING

The observational studies on the comparative clinical effectiveness of DXA and other technologies to discriminate the fractured from the non-fractured were variable regarding the technologies used, the outcome measures reported, and the patient population. Most studies reported results as AUC after ROC analysis. One study did not report AUC. The AUC for DXA ranged from 0.59 to 0.95 for the different bones analyzed across the studies. QUS AUC ranged from 0.60 to 0.93, and QCT ranged from 0.87 to 0.93 in the studies. There do not seem to be differences between DXA and QUS in the studies, except in one study, which showed SOS AUC to be lower than DXA AUC. The BUA AUC, however, was similar to the DXA in this study.[9] The study comparing MDCT with DXA showed a higher AUC for MDCT compared with DXA, which may indicate that MDCT is a better screening test than DXA for predicting fracture risk.[11] ORs for predicting fracture risk were reported for four of the six studies and ranged from 1.35 to 4.8 for DXA, from 1.26 to 4.18 for QUS, and 12.7 to 16 for QCT. There are no differences between the ORs in the studies, except in the study on MDCT and DXA, where the OR is higher for MDCT compared with DXA.[11] One study reported hazard ratios, which were similar between DXA and QUS.[13]

Three studies examined the costs of bone densitometry testing. One study from Thailand converted costs to US dollars. The cost-effectiveness ratio per fracture prevented for DXA was US$88.42 and US$146.48 for QUS. The ICER was US$79,930 for DXA and US$137,990 for QUS. In this study, QUS was more costly than DXA. The US study found the costs per 1,000 patients to be US$703,000 to prevent 7.8 fractures for DXA compared with US$632,000 to prevent 6.7 fractures for QUS and US$442,000 to prevent 5.7 fractures using a sequential approach of QUS followed by DXA. The Spanish study found the total costs of DXA were €3,554 and €3,211 for QUS, with the average cost per case detected to be €22.85 for DXA and €22.00 for QUS. The costs for DXA and QUS were similar in these two studies. It is unknown, however, whether any of these studies could be translatable to a Canadian setting.

There were limited data on other technologies, such as radiology and QCT, for the prediction of fracture risk. One study assessed radiology, and two studies assessed QCT. QCT seems to be at least as effective as DXA. QCT, however, uses more radiation than DXA. Based on the literature reviewed, QUS seems to be comparable to DXA for the prediction of fracture risk in postmenopausal women, although this is based on low quality evidence from retrospective and prospective observational studies. It is unclear whether these technologies would be used with DXA or to replace DXA. Other factors such as the lack of radiation used for QUS and the limited availability of DXA may help to determine which screening test would be most useful. None of the studies included was Canadian, and more research is needed to make an informed decision regarding methods to measure bone densitometry in postmenopausal women.

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