Improving Clinical Decisions for Women at Risk of Osteoporosis: Dual-Femur Bone Mineral Density Testing

Raymond E. Cole, DO, CCD

Context: In bone mineral density (BMD) testing, unilateral hip analysis and lumbar spine measurement have been the clinical standard for diagnosis and treatment classification for postmenopausal women at risk of osteoporosis.

Objective: To determine if analysis of the bilateral hip in BMD testing has a clinical effect on diagnosis of osteoporosis and treatment classification of patients.

Methods: Dual-femur BMD test results from 313 postmenopausal women (mean age 61.2 years, range 32-90 years) were evaluated using standard BMD reference values for diagnosis and treatment classification. The author compared T scores for right and left femurs at three sites: femoral neck, trochanter, and total femur.

Results: When the bilateral hip was considered in BMD testing and compared with unilateral hip results, a clinical change in diagnosis from normal to osteopenia occurred in 5.7% of subjects. In addition, a clinical change in diagnosis from osteopenia to osteoporosis occurred in 3.3% of subjects. A clinical change in treatment classification from “no treatment required” to “treatment required if one or more risk factors are present” occurred in 3% of subjects. A change in treatment classification from “treatment required if one or more risk factors are present” to “treatment required independent of risk factors” happened in 2.4% of subjects.

Conclusion: When compared with BMD testing of the unilateral hip, inclusion of the bilateral hip in BMD testing resulted in a change in classification to a more severe diagnosis in a total of 9% of subjects, and to a more aggressive treatment category in a total of 5.4% of subjects. Dual-femur BMD testing may improve diagnosis and treatment classification for postmenopausal women at risk of osteoporosis.

The official position of the International Society for Clinical Densitometry (ISCD) is that bone mineral density (BMD) should be measured at both the posterior-anterior spine and the hip in all patients when a central dual-energy x-ray absorptiometry (DXA) measurement is performed.1,2 The 1994 World Health Organization (WHO)3 diagnostic criteria for osteopenia and osteoporosis focused on BMD measurements at the unilateral hip (ie, either the right or left proximal femur), which was the best technology available for analysis at the time. The WHO criteria became the accepted clinical standard.

Since 1994, however, new technology—dual-femur BMD testing, in particular—has become available, allowing rapid BMD scanning of the bilateral hip (ie, both the right and left proximal femurs) in a single acquisition.

A question of clinical relevance that must be answered is:

What effect does dual-femur BMD testing have on diagnosis classification (normal, osteopenia, or osteoporosis) and treatment classification (no treatment required [NTR], treatment required if one or more risk factors are present [TR1], or treatment required independent of risk factors [TR]) for postmenopausal women at risk of osteoporosis?

Bonnick et al4 concluded that dual-femur BMD testing may not be clinically necessary. Their study,4 however, was limited because it examined the effect of only total-femur BMD (g/cm²) on diagnosis classification in premenopausal women (mean, 32.9 y; SD, 18 y), without analyzing the diagnostic value of the T scores from individual femoral sites in postmenopausal women. The T-score system is used for diagnosis classification by comparing an older patient’s BMD with the optimal peak (ie, young adult) BMD for that patient’s gender.3 The T scores are reported as the number of standard deviations below the young adult mean (normal, > -1; osteopenia, -1 to -2.49; osteoporosis, ≤ -2.5).3 Bonnick et al4 used a Z score of less than -1 as the criterion for determining that a patient was at risk for osteoporosis. The Z-score system compares a patient’s BMD with results from other individuals of the same age, weight, ethnicity, and gender.4 Another limitation of the study by Bonnick et al4 was that it did not investigate how dual-femur BMD testing was related to treatment classification.
Mazess et al\(^5\) addressed the use of dual-femur BMD testing in postmenopausal women. They concluded:

...bilateral [hip] measurements might be particularly useful in older patients, or in those with lower femoral BMD, to compensate for the poorer precision of unilateral measurements. The dual-femur approach may prove useful to better address the risk of osteoporotic fracture in clinical practice as well as research. The dual-femur measurement, which takes only a few minutes more of patient time than the standard single-femur determination, reduces uncertainties in critical skeletal region.\(^5\)

Balseiro et al\(^6\) also reported on the value of dual-femur measurements. They found that “the asymmetry of BMD is due to real differences between hips. Therefore the BMD of one hip cannot be used to predict that of the other with sufficient accuracy to discriminate clinically relevant trends in BMD.”\(^6\) Thus, they recommended that DXA testing be performed on both the right and left hips, at least on the patient’s initial examination.\(^6\)

By contrast, Petley et al\(^7\) concluded that data from dual-femur measurements “suggest that there is only a small benefit from performing bilateral femoral neck BMD measurements.” Yet, it is important to note that the study by Petley et al\(^7\) was limited in that it examined only how dual-femur BMD testing changed diagnoses to osteoporosis. In addition, Petley et al\(^7\) measured only the femoral neck BMD and did not include BMD measurements of the total hip or trochanter, nor did they examine diagnosis classification changes from normal to osteopenia or changes in treatment classification.

To assist in answering the question as to whether there is clinical value in performing bilateral hip analysis of BMD rather than only unilateral hip analyses in postmenopausal women, the present study examined subjects’ bilateral hip BMD measurements and compared T-score values obtained from different femoral sites. The primary objective of this analysis was to determine if the inclusion of measurements from the bilateral hip in BMD testing alters subjects’ clinical diagnosis and treatment classification when compared with unilateral hip measurements. The present study addresses the clinical significance related to research findings from a previous study\(^8\) that explored the differences in BMD between the right and left hip as measured by dual-femur BMD testing.

### Materials and Methods

#### Reference Samples

A retrospective review of patient medical records was undertaken. The patient records of 313 postmenopausal white (non-Hispanic) women who received dual-femur BMD testing at an osteoporosis testing center between August 6, 1999, and May 16, 2001, were analyzed. The right and left femur T-score results of these individuals were analyzed to determine if inclusion of the bilateral hip T score made a difference in diagnosis and treatment. The study population consisted of those individuals who had signed informed consent and HIPAA (Health Insurance Portability and Accountability Act) authorization forms to allow their BMD data to be used in research. Study subjects were among a random population of some 1200 postmenopausal women referred to the testing center by physicians who deemed the individuals to be at risk for osteoporosis. The Michigan State University Committee on Research Involving Human Subjects (East Lansing) approved all aspects of the present study.

The WHO\(^3\) diagnostic criteria published in 1994 and the National Osteoporosis Foundation (NOF)\(^9\) treatment recommendations guidelines published in 1998 both addressed only postmenopausal white women. Thus, only postmenopausal white women were included in the subject sample for the present study. The subjects included women who were postmenopausal not only because of age, but also because of the surgical removal of their ovaries. Women receiving antiresorptive therapies, including hormone replacement, were also included in the present study. Premenopausal women, non-white women, men, and children were excluded from the present study. Also excluded from study were women with a medical history of glucocorticoid medication use, stroke with hemiplegia, and physical limitations as a result of limb immobilization or osteoarthritic conditions.

As noted, study subjects were women referred to the osteoporosis testing center based on the clinical judgment of their treating physicians after evaluation of their osteoporosis risk factors. Referrals were obtained from 21 different physicians, including specialists in family practice, internal medicine, obstetrics and gynecology, orthopedics, and rheumatology. Five of these physicians were osteopathic physicians. Because the population used for the current study is subject to selection bias—in particular, referral bias—the conclusions that can be drawn as a result of this research are limited to postmenopausal white women who are at risk for osteoporosis.

### Bone Density Measurements

Dual-femur DXA measurements of BMD were performed using a bone densitometer device (Lunar Prodigy; GE Healthcare, Milwaukee, Wis) with population reference software (Lunar North American 2.05.038; GE Healthcare, Milwaukee, Wis). The tests were performed by a technician certified as both a densitometry technician by the ISCD and as a technologist in diagnostic radiology by the American College of Radiology. The BMD scans were interpreted by an ISCD-certified clinical densitometrist (R.E.C.).

Reference data obtained from dual-femur analyses were converted into T scores. Comparisons of T scores from the bilateral hip were made with T scores from the unilateral hip to determine if the bilateral T scores resulted in differences in diagnosis and treatment categories.

The present study included T scores derived from BMD measurements.
measurements taken at three different hip sites: the femoral neck, greater trochanter, and total proximal femur (Figure). The selection of these three sites followed the diagnostic and therapeutic intervention thresholds that were standard in the United States at the time of data analysis (ie, 2004). These thresholds were based on the clinical use of the lowest T score from any of three regions of interest (ROI), as defined by the ISCD: the femoral neck, greater trochanter, or total proximal femur. The ISCD criteria also noted that BMD measurements from the Ward’s triangle should not be used for diagnosis. In 2005, the ISCD revised its clinical criteria to include the use of the lowest T score obtained from either the femoral neck or total proximal femur only; T scores from the trochanter are no longer to be considered. Lumbar spine BMD measurements were obtained using the standard ISCD criteria for measurement of L1 through L4.

Precision error for BMD measurements at the right and left hip was determined by using data from 30 subjects, according to standard ISCD protocols. Precision error at the femoral neck, trochanter, and total femur was 1.39%, 1.80%, and 1.03%, respectively. The least significant change with 95% confidence at the femoral neck, trochanter, and total femur, expressed as root mean square standard deviation (RMS SD), was 0.034 g/cm², 0.039 g/cm², and 0.028 g/cm², respectively.

**Diagnosis and Treatment Reference Values**
The standard WHO reference values established for BMD measurement in white women were used to define normal BMD, osteopenia, and osteoporosis diagnoses classifications:

- normal, > -1
- osteopenia, -1 to -2.49
- osteoporosis, ≤ -2.5

The standard reference values for pharmacologic treatment of patients with osteoporosis developed by the NOF for postmenopausal white women were used to define treatment classifications:

- TR, ≤ -2
- TR1, -1.5 to -2
- NTR, ≥ -1.5

The present study did not evaluate whether risk factors were actually present in subjects.

**Results**

**Subject Characteristics**
The demographic characteristics of the 313 subjects participating in the current study are presented in Table 1. The mean age of subjects was 61.2 years, with a range of 32 to 90 years. Mean (SD) subject height was 160 cm (63.1 in); weight, 73.9 kg (163 lb). As previously noted, all subjects were postmenopausal white women.

**Figure.** The anatomy of the hip region, including the head, femoral neck, greater trochanter, and lesser trochanter of the proximal femur, and the acetabulum, ilium, ischium, and pubis of the os coxae (pelvic bone).

Raymond E. Cole, DO, CCD, derived measurements of bone mineral density (BMD) from three sites: the femoral neck, greater trochanter, and total proximal femur (including neck, greater trochanter, and lesser trochanter). Inclusion of the bilateral hip in BMD testing resulted in a change in classification to a more severe diagnosis in a total of 9% of subjects, and to a more severe treatment category in a total of 5.4% of subjects, compared with results achieved using BMD testing of the unilateral hip. Dual-femur BMD testing may improve diagnosis and treatment classification for postmenopausal women at risk of osteoporosis.
The mean T scores for subjects were -0.959 for the right hip, -0.943 for the left hip, and -0.785 for the lumbar spine. In 121 subjects (38.6%), the spine T score was lower than the lowest hip T score. The average absolute difference in T scores between the left hip and spine, compared with the right hip and spine, was 0.36. The average absolute difference in T scores between the right and left hips as measured at the femoral neck was 0.34; at the trochanter, 0.38; and for total femur, 0.29.

The BMD measurements from both hips and the spine indicated that, when all three structures were analyzed, 113 subjects (36.1%) met the diagnostic criteria for normal bone density, 146 (46.5%) had osteopenia, and 54 (17.4%) had osteoporosis. As a result, 185 subjects (59.2%) received a bone density, 146 (46.5%) had osteopenia, and 54 (17.4%) had osteoporosis. As a result, 185 subjects (59.2%) received a diagnosis classification change from normal to osteopenia in 36 subjects (11.4%), and from osteopenia to osteoporosis in 21 subjects (6.6%). A change in treatment classification to a more severe category occurred in a total of 28 subjects (9%)—approximately 1 in 11 subjects—when the bilateral hip was included in BMD testing (Table 2).

**Effects on Clinical Diagnosis**

When the lowest T score from the different site-specific measurements made in the bilateral hip analysis was compared with the lowest T score from a unilateral hip analysis of both the left and right hips, the treatment classification changed from NTR to TR1 in 19 subjects (6%). Treatment classification changed from TR1 to TR in 15 subjects (4.7%). In this scenario, a change in treatment classification to a more severe category occurred in a total of 33 subjects (10.7%).

As with clinical diagnosis, the “correct,” or lowest, T score from the two hips is likely to be found in unilateral hip analysis and used for treatment classification 50% of the time in clinical practice. When this limited success rate was taken into account, the treatment classification obtained from the bilateral hip analysis—compared with unilateral hip results—changed from NTR to TR1 in 9 subjects (3%). Treatment classification changed from TR1 to TR in 7 subjects (2.4%). Thus, in this scenario, treatment classification changed to a more severe category in a total of 16 subjects (5.4%)—approximately 1 in 19 subjects—when the bilateral hip was included in BMD testing.

In summary, inclusion of the bilateral hip in BMD testing made a clinically meaningful difference in diagnosis classification in 28 subjects (9%) and in treatment classification in 16 subjects (5.4%).

**Comments**

Total-femur BMD (g/cm²) is highly correlated between the right and left hips.4,10-18 It must be kept in mind, however, that comparing the total-femur BMD between hips does not reflect the site-specific T-score variations that are crucial for accurate osteoporosis diagnosis and treatment classification.
The WHO\textsuperscript{3} diagnosis classifications and the NOF\textsuperscript{5} treatment classifications are based on the lowest T score from the lumbar spine and the lowest T score from among the ROI sites of the femur (femoral neck, trochanter, total femur prior to 2005; femoral neck, total femur post-2005)\textsuperscript{6} of either hip.

Kasalicky and Rosa\textsuperscript{7} examined T-score differences between the right and left hips at the femoral neck and total femur in a population of postmenopausal Czech women. They reported that diagnosis classification differed between the right and left hips in 29\% of subjects (16\% at the femoral neck, 13\% at total femur). Cole and Larson\textsuperscript{8} demonstrated that diagnosis classification differed between the right and left hips at the femoral neck and total femur (femoral neck, trochanter, total femur prior to 2005; femoral neck, total femur post-2005)\textsuperscript{9} of either hip.

Petley et al\textsuperscript{10} examined how femoral neck BMD measurements of the bilateral hip affected diagnosis classification changes from osteopenia to osteoporosis, concluding that measuring the BMD of both right and left femoral necks was beneficial for the diagnosis of osteoporosis in only a small number of cases (51 of 2372 [2.2\%]). However, their study\textsuperscript{10} was limited for various reasons, as previously noted, including the fact that it examined only the femoral neck and did not include BMD measurements of the total hip or trochanter.

DeFrancisco et al\textsuperscript{20} examined the usefulness of including BMD measurements from the bilateral hip when either the spine or initial hip measurement has a BMD value consistent with osteoporosis and the other measurement does not. They concluded that, in this clinical situation, there is not sufficient clinical advantage to include data from the second hip.\textsuperscript{20} However, their study examined only diagnosis classification changes to osteoporosis without considering changes from normal to osteopenia or treatment classification changes.

Gnudi and Malavolta\textsuperscript{21} examined the T-score–based diagnosis of osteoporosis in 1200 postmenopausal women at the spine, femoral neck, trochanter, and Ward’s triangle. Their study demonstrated that differences in T scores at each of these sites resulted in diagnostic inconsistencies.\textsuperscript{21} Like DeFrancisco et al,\textsuperscript{20} Gnudi and Malavolta\textsuperscript{21} specifically analyzed diagnosis classification changes to osteoporosis without analyzing changes from normal to osteopenia or treatment classification changes. Prior to the present study, no clinical studies have focused on the total diagnostic and treatment implications of inclusion of the bilateral hip in BMD testing.

In accord with the results of other researchers,\textsuperscript{7,20,21} the present study found that when the bilateral hip is included in BMD testing, the percentage of subjects moving from a diagnosis of osteopenia to osteoporosis is relatively small (3.3\% in the present study). However, from a comprehensive clinical perspective, the total effect on the clinical management of the patient is noteworthy when one considers diagnosis classification changes (from normal to osteopenia in 5.7\% of subjects, and from osteopenia to osteoporosis in 3.3\% of subjects) and treatment classification changes (from NTR to TR1 in 3\% of subjects, and from TR1 to TR in 2.4\% of this population).

The present study clearly demonstrates that site-specific differences in BMD and subsequent T scores derived from examination of the bilateral hip may result in changes in diagnosis or treatment classification in BMD testing from those derived using only BMD measurements from the unilateral hip. Dual-femur BMD testing may help reveal these differences, thereby increasing the sensitivity of BMD analyses of patients who are at risk of osteoporosis.

The dual-femur DXA scan presents an important diagnostic consideration for physicians in the clinical setting. At the time the WHO\textsuperscript{3} diagnostic criteria were developed, acquisition of data from the unilateral hip was the best technology available. Consequently, this technology became the accepted clinical standard, and diagnosis and treatment recommendations were based on a single-femur measurement. The present study indicates that the use of dual-femur BMD measurements would increase the observed prevalence of osteoporosis, thereby invalidating the criteria for the WHO\textsuperscript{3} definition of osteoporosis based on BMD measurements of the unilateral hip in postmenopausal white women.

**Clinical and Ethical Questions**

It is possible to argue that because dual-femur BMD testing increases the probability for diagnosis of osteoporosis and subsequent treatment of patients, this testing may result in overdiagnosis and overtreatment. Any time multiple skeletal sites rather than a single site is used for BMD measurements, the parameters for diagnosis and treatment are increased. Thus, the following question is raised: Where is the correct line for clinical diagnosis and treatment classification to be drawn? The answer to this question is complex, involving more than just the inclusion of the bilateral hip in BMD testing.

For example, if we normally measure BMD in just one hip for diagnostic purposes, are there still circumstances in which the bilateral hip measurement should be included? When should BMD measurements from other ROI sites, such as the forearm, be included? What effect does vertebral fracture analysis have on the diagnosis and prevalence of osteoporosis, as defined by the WHO criteria? Should the mean hip BMD, rather than the lowest hip BMD, be used for diagnosis and treatment stratification? If so, should measurements from the femoral neck or total femur be used to calculate the mean?

A sound, rational argument can be made for investigating each of these considerations. Yet, the most important fact to remember is this: If patients are at risk for fracture, they need to be identified, diagnosed, and treated—whether through the use of dual-femur DXA scans, vertebral fracture analysis, or another testing method.

The present study also raises several ethical questions. Are the clinical discrepancies stemming from unilateral hip testing vs bilateral hip testing acceptable in light of today’s
advanced technology? Can physicians have full confidence in their diagnosis and treatment recommendations when performing a unilateral hip test? Can physicians be certain that their patients are not being underdiagnosed or undertreated when the BMD from only one femur is measured? Could underdiagnosis resulting from unilateral hip testing be one of the intangibles as to why some individuals fracture with little trauma despite having apparently “normal” BMD?

Underdiagnosis can have serious consequences for a patient when it results in a conservative, wait-and-see approach to patient treatment instead of aggressive treatment to prevent fracture and other conditions related to BMD loss. The importance of a correct diagnosis of osteoporosis is magnified in the first 5 years of menopause because of the accelerated BMD loss of approximately 2% to 3% a year that a woman typically experiences during this time. Thus, during the course of a woman’s life, a physician’s diagnosis may mean the difference between a severe fracture and strong, healthy bones. Would a substantial number of lives be saved, and would morbidity be decreased, by the widespread use of dual-femur BMD testing to diagnose fracture risk?

Limitations

One of the limitations of the present study is that it is not a fracture-outcome study, so it does not correlate the gradient for the risk of fracture with less severe categorization of diagnosis. Another limitation, as previously noted, is that the subjects were selected from a random clinical population of postmenopausal women referred to an osteoporosis testing center because they were deemed by their physicians to be at risk for osteoporosis. Thus, this study is not representative of the general population of postmenopausal women.

Yet another limitation is that the present study relied on the Lunar Prodigy (GE Healthcare, Milwaukee, Wisc) population database for North American women, which was the standard database at the time of the study, rather than the current standard population database for North American women—the Third National Health and Nutrition Examination Survey (NHANES III). The subjects in the present study had densitometry studies performed prior to the reference NHANES III database becoming the standard in 2005. Finally, this study did not evaluate—nor can any conclusions be drawn about—whether diagnosis and treatment categorization should be based on the lowest hip T score or the mean T score obtained from dual-femur BMD testing.

Conclusions

Dual-femur BMD testing may improve clinical decisions in diagnosis and treatment classification for postmenopausal women at risk of osteoporosis. This technology allows rapid BMD scanning of both hips in one acquisition, eliminating time-consuming repositioning of the patient and minimizing the patient’s exposure to radiation.

The results of the present study show that inclusion of the bilateral hip in BMD testing made a difference in diagnosis classification for 9.0% of subjects and treatment classification for 5.3% of subjects. These differences warrant clinical consideration of performing dual-femur BMD testing for all postmenopausal women.

Questions that remain to be investigated in future studies include the following:

- To what degree will dual-femur BMD assessments result in improved clinical status of patients through the reduction of fracture rates?
- Should mean T scores for bilateral hip BMD testing be used for diagnosis and treatment decisions?
- Which ROI sites provide the best predictive ability for osteoporotic fracture, including hip fracture?

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References


