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Bone Mineral Densitometry Measurement

Girls to Women

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Abstract

Bone mineral densitometry (BMD) can be performed in any age group. Originally, BMD was utilized in elderly postmenopausal women for whom World Health Organization criteria for diagnosis of osteoporosis were determined. With the proliferation of treatment options for low bone mass, the utilization of BMD measurement has increased. In the premenopausal female BMD use and interpretation must be judicious and correlated to clinical findings. Children present a number of problems in the use and interpretation of BMD. Dual-energy X-ray absorptiometry remains the gold standard for measurement of BMD.

Key Words: Bone mineral densitometry; T-score; least significant change.

Introduction

Osteoporosis is a skeletal disorder characterized by compromised bone strength predisposing to an increased risk of fracture where bone strength reflects bone density and bone quality *(1)*. Bone mineral densitometry (BMD) techniques were developed to identify individuals with low density who are at risk for fracture and in whom treatment may prevent fracture. BMD is the best predictor of fracture risk at this time *(2,3)*.

Bone densitometry is performed to (a) determine the need for prevention or treatment of low bone density, referred to as osteopenia and osteoporosis; (b) aid the patient in deciding to initiate treatment; (c) assess for fracture risk; and (d) evaluate efficacy of treatment *(4)*. Two methods are used clinically to determine bone density. The gold standard for densitometry today is dual-energy X-ray absorptiometry (DXA). Quantitative computed tomography (QCT) identifies individuals with low bone density. Both techniques can provide information regarding fracture risk. Quantitative ultrasound (QUS), radiodensitometry, peripheral DXA, peripheral QCT (pQCT), and single-energy X-ray absorptiometry (SXA) are used to determine individuals at risk for fracture. Bone architecture can be assessed to determine trabecular connectivity and trabecular volume using magnetic resonance (MR) and micro-CT *(5)*.

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Overview of BMD Evaluation

Certain measurements and statistical information are provided by BMD. DXA provides an areal bone density in grams per centimeter squared (g/cm^2). A statistical assessment known as a T-score is provided. The T-score is a comparison of the BMD of the individual compared with a reference group at peak bone density, between ages 20 and 30 depending on the scanner *(6)*. For each standard deviation below the mean of the young adult reference data, an approx

10% loss of bone density occurs and a doubling of fracture risk is realized *(7)*. T-scores can take into account race and height for comparison with the reference data. The International Society for Clinical Densitometry's (ISCD) official position is to use a uniform Caucasian non-race-adjusted database for women of all ethnic groups in the United States. World Health Organization (WHO) diagnostic criteria uses T-scores. WHO diagnostic criteria for osteoporosis was originally determined by evaluating elderly, postmenopausal Caucasian females. T-scores are used for diagnosis of osteopenia and osteoporosis. A T-score of −1.0 and above is normal. A T-score between −1.0 and −2.5 signifies osteopenia. Osteoporosis defined by BMD is indicated by a T-score of −2.5 and below; severe osteoporosis is −2.5 and below with a fragility fracture *(8)*. WHO criteria are used for spine, hip, and forearm DXA scans. The lowest T-score at any site of the spine or hip (femoral neck, trochanter, or total) is used for diagnosis *(9)*. Discordance between anatomic sites evaluated by DXA occurs for multiple reasons, including the percentage of cortical and trabecular bone present *(10,11)*. Follow-up scans compare spine or total hip density in g/cm^2, not T-scores, to determine stability or change in BMD. Current applications will be discussed later in this section. The DXA T-score is also used to determine fracture risk. T-scores are provided by other density technologies, but they are used for fracture risk evaluation, not diagnosis, and they are not equivalent to DXA T-scores *(12)*.

A Z-score is also provided with BMD. This statistical measure provides information regarding the comparison of the individual to their age matched peer group. Z-scores are also race- and height-matched. Z-scores are used for several reasons. Identifying patients with possible secondary causes of low bone density/osteoporosis (≤ 2.0 S.D. below the mean for the reference data) is one (ISCD). Secondary causes of low bone density can be present without a significantly abnormal Z-score *(13)*. Second, there are proponents of using the Z-score to determine fracture risk. Z-scores are reported only for pediatric and premenopausal BMDs.

Technologies

DXA utilizes two X-ray energies. The higher-energy X-ray is attenuated by soft tissue and bone approximately equally. A second, lower-energy X-ray is attenuated differently by bone (more attenuation) than soft tissue. The difference in absorption between the two X-ray energies is subtracted and compared to reference data, and a BMD is calculated. Radiation dose is very low: 1 to 5 microsieverts for BMD and slightly higher for vertebral fracture assessment. Accuracy of DXA is 4 to 10% and consistent with a properly functioning scanner *(14)*. Precision (reproducibility) of DXA scanners with a phantom is approx 1% *(15)*.

DXA BMD requires the operator and interpreter to pay attention to quality assurance (QA) issues. Daily QA is performed. On a modern scanner the data for QA are recorded and graphed. Changes in the consistency in generation of X-rays and alignment of mechanically moving parts can be detected by a sudden shift in QA parameters. Drift in QA occurs as the result of aging of equipment and environmental influences. QCT has different QA measures from DXA.

Least significant change (LSC) must be determined. LSC determines the range of variation that establishes the density changes required to ensure a real change in BMD on serial scans. LSC is determined by scanning 15 patients three times each or 30 patients two times each with repositioning between scans. The patients should be representative of the age range seen in the practice. LSC is the variability in scan acquisition resulting from positioning and analysis by the technologist, including the inherent variability of the scanner. Region of interest (ROI) placement and positioning must be evaluated on the initial scan. The interpreter must pay attention to the area changes, positioning, and placement of the ROI on sequential scans. Changes in area and ROI of more than 2% between scans and different positioning can significantly and falsely change BMD, which will have the appearance of increase or decrease in BMD *(16)*.

LSC and the expected outcome of treatment determine the follow-up period for BMD. Until recently most treatments did not increase BMD greater then LSC in less than a 2-yr period. Therefore, the Medicare reimbursement schedule allows for DXA for monitoring treatment every 2 yr *(17)*. To demonstrate a change in BMD, the change must exceed the LSC. If BMD does not increase but remains stable, i.e., does not exceed BMD in a positive or negative

value, then the treatment is considered effective. The exceptions to monitoring BMD more frequently include hyperparathyroidism, treatment with steroids, or treatment with a medication that rapidly increases BMD.

Interpreters are also responsible for identifying confounding factors that will adversely affect BMD assessment. Removal of vertebral bodies with significant degenerative changes should occur. Degenerative changes of the hip that affect the femoral neck measurement should be noted *(18,19)*. Any abnormal appearance on the scan, which is not a diagnostic X-ray, should result in the interpreter suggesting additional radiographic evaluation.

QCT can be performed on a computerized tomography scanner. QCT also measures attenuation of X-rays. Software must be purchased, including a phantom. Phantoms are used for QA and to determine regression curves that correlate BMD to Hounsfield units. The software provides analysis for BMD of generally two to four vertebrae. Analysis can be performed using only trabecular bone or can include cortical bone, unlike DXA, which measures both components of bone and includes posterior elements. QCT provides a volumetric BMD; therefore, the measurements are not affected by the size of the bone. Density is expressed as grams per centimeter cubed (g/cm^3). Databases are provided for QCT measurements. The QCT-derived T-score is not equivalent to the DXA T-score and cannot be used to diagnose osteoporosis. QCT T-scores cannot be used to determine osteoporosis using WHO diagnostic criteria. The only determination that can be made using QCT is that BMD is low compared with the reference database on the initial scan. Serial scans can be used to determine changes in BMD in treated patients because of the increased sensitivity to change of trabecular density. QCT has poorer precision than DXA (1.5 to 4%). Automated analysis and use of spiral CT reduce error and improve precision on serial scans. Reference databases are available for age, sex, and race *(20)*. Volumetric BMD *(21)* of the proximal femur has recently been approved by the US Food and Drug Administration (FDA) and offered by one software manufacturer.

Peripheral densitometric techniques are variable in technology. Ultrasound has been used to evaluate multiple anatomic sites *(22,23)*. Heel ultrasound is the most commonly used peripheral modality. Heel densitometry is portable and uses no X-rays. Sound wave transmission through the heel is affected by the number and architecture of the trabecula and the amount of mineralization present. Mineralization can be correlated to normal reference data but the effect of architecture changes cannot be determined at this time. T-scores are not equivalent to DXA but can predict fracture risk globally *(12)*. An individual at risk for fracture still needs a DXA for baseline and to follow treatment if necessary. Heel ultrasound cannot be utilized to follow patients on treatment. Other technologies utilize X-rays and are much less commonly used in the United States; these include radiodensitometry, SXA, and pQCT.

Densitometry measurement can be performed at any age. The reason for performing the scan in any individual other than a postmenopausal female, however, must be clearly defined. Fracture risk based on BMD is not established for infants, children, or premenopausal women. It is a gradient; consequently, risk increases significantly with age for the same T-score. When determining fracture risk in premenopausal females, clinical risk factors are most important.

BMD in Infants and Children

The only reason to perform BMD in infants at this time is for research. There is no database for comparing an infant DXA BMD. QCT and pQCT reference data for the forearm have been established for infants and children *(24)*. pQCT is not commonly used in the United States. No fracture risk information is available for infants. For purposes of research, DXA total body (whole body) BMD (TB-BMD) must be used *(25)*. The initial scan is the baseline used to follow BMD. Because the infant is expected to grow, overall density will be affected less by changes in bone size, as it can be adjusted for area. BMD by DXA is calculated by dividing bone mineral content by the area of the bone region of interest. The result is an areal measurement, g/cm^2. If density remains constant and the area changes either by incorrect positioning of the patient or the different ROI, an increase in area will result in an apparent decrease in BMD and a decrease in area will appear to increase BMD. A site-specific area measurement change will significantly affect BMD more than area changes of a TB-BMD.

QCT has been proposed for assessment of infant BMD because it is a volumetric measurement and not dependent on bone size. The problem with using this assessment is that infant vertebrae are largely cortical bone. A large enough ROI for adequate precision, trueness of sequential measurements, is very difficult or impossible to achieve. More important, the radiation dose is high compared with that for other techniques.

Toddlers and children, up to the age of peak bone density, can be evaluated using DXA TB-BMD, spine and hip BMD. The manufacturer's reference database for children is limited and begins at age 4 to 17. Hip BMD has a database from a specific manufacturer that is not available on the scanner. Published databases exist. The problem here is that these databases are limited to a specific scanner and, more important, they were established on pencil beam scanners. Data collected on one version of software and a specific scanner can be compared only to other data from the same scanner model. Because many scanners are now fan beams, the pencil-beam database has no comparative value. In addition, the data cannot be used for scans from another manufacturer.

BMD has been corrected for area, height, bone age, and lean body mass. No agreement exists at this time regarding the best method to correct for BMD in children who are ill, of different ethnic groups, small, or those who have delayed growth *(26–28)*.

Once the bone has stopped growing the density changes are easier to evaluate assuming the same size and position of the ROI. Vertebrae secondary growth centers fuse between 15 and 25 yr of age in females. Vertebral peak bone density may peak between approx 15.7 and 23 yr of age. Epiphysis and apophyses of the hip fuse at different chronologic ages. Peak bone density of the femoral neck and trochanter occurs between 14 and 18.5 yr *(6,29)*.

The Z-score is used to evaluate the BMD. A single point analysis does not ensure an accurate assessment of BMD for diagnosis, only a relative reference point in time. To determine low bone density the Z-score must be −2.0 or lower *(16)*. There is disagreement as to how a BMD should be analyzed. Instead of chronologic age investigators have used skeletal age, height age, and Tanner stage age to analyze the BMD to correct for factors not taken into account by the reference database *(28)*.

Clinical decisions to treat should not be made based on BMD alone, other than usual nutritional recommendations for calcium and vitamin D. Serial BMDs are difficult to assess, as the bone will enlarge as the child grows. Determining increase in serial BMD is not completely reflected by g/cm^2. The area and bone mineral content (BMC) changes need to be taken into account. Centile curves of bone area for age BMC for age, bone area for height, and BMC for bone area have been determined when TB-BMD is utilized *(25)*.

Fracture risk cannot be determined using BMD in infants or children. No data exist that correlate a BMD to a fracture risk. Clinical factors associated with fracture risk should be evaluated independent of BMD.

Except for patients treated with steroids, who should be scanned every 6 to 12 mo until stable, there is no specific recommendation for intervals between scans in pediatric patients. Indications for measuring BMD in the pediatric population are the presence of established secondary causes that can decrease bone mass. Secondary causes include nutritional disorders, metabolic diseases, and steroid treatment. Children with parents who have low bone density are likely to have low bone density themselves. Fifty percent of low bone density is secondary to genetics. Children who fracture have low bone density. Women who had low bone density as children are at higher risk for a postmenopausal fracture.

Key Points: BMD in Children

1. BMD for children should performed only if there is a suspected or known secondary cause of low bone density.
2. The Z-score is used to determine low bone density (−2.0 or lower).
3. Serial scans are difficult to assess for significant changes.
4. Treatment decisions should not be made based on BMD alone.

BMD in Premenopausal Women

Peak bone density is achieved between the ages of 20 and 39 yr. Bone density decreases from peak at a rate of approx 0.5 to 1.0% per year. Age-matched reference databases have been developed for premenopausal women. ISCD position statements recommend using Z-scores to determine low

bone density for premenopausal women *(16)*. Z-scores of −2.0 S.D. or lower below the mean for age-matched data are considered low. Low bone density in a premenopausal woman on a single study should be interpreted realizing that this is only a snapshot of bone health. One measurement does not answer whether the patient ever reached peak bone density. Low density needs to be correlated by the primary care physician with clinical, social, and environmental factors to determine the need treatment. Measurement of BMD in premenopausal women should not be requested unless there is a secondary cause of low bone density suspected or present, and should not be done in pregnant women. Secondary causes for low bone density are numerous and include treatment with steroids, medications associated with decreased BMD, metabolic bone diseases, and other diseases whose presence or treatment result in low bone density. Osteoporosis is not diagnosed in premenopausal women based on BMD *(16)*.

BMD in Postmenopausal Women

Postmenopausal BMD assessment is well delineated. Two types of postmenopausal patients are evaluated. Patients over 65 yr old have had guidelines for BMD established by Medicare *(17)*; these include estrogen deficiency at risk for osteoporosis, radiographic evidence of osteopenia or osteoporosis with fracture, long-term treatment with corticosteroids, primary hyperparathyroidism, and assessment of treatment with an FDA-approved medication. Peripheral densitometry is reimbursed by Medicare as a separate Current Procedural Terminology (CPT) code; in the first year of identifying fracture risk a central scan will be reimbursed. Scans can then be performed every 2 yr to monitor treatment. If the patient is treated with steroids, BMD can be reimbursed more frequently with appropriate documentation (recommended every 6 to 12 mo). The guidelines have been adopted by many insurance companies and also apply to younger postmenopausal women. Each state's reimbursement varies. Prior to performing BMD on the pre-65-yr-old postmenopausal woman, reimbursement should be established so that the patient may be informed of her financial responsibility.

In addition to the Medicare guidelines, other reasons for obtaining BMD studies are extensive, including metabolic bone disease, other diseases, and medications *(30)*.

Watts *(31)* noted that trabecular bone loss is accelerated in postmenopausal women, whereas cortical bone loss occurs at a slower rate unless a secondary cause of low bone density is present.

Spine and hip scans (femoral neck, trochanter, total hip regions of interest) are obtained. The reason for two scan sites is to ensure that at least one site will be available for follow-up studies. The spine is predominantly trabecular bone and changes in BMD are detected earlier at this site. Hip BMD has a larger component of cortical bone that is evaluated; therefore, changes in BMD occur more slowly with osteoporosis. Diagnosis of osteopenia/osteoporosis using the WHO criteria is made on the lowest BMD at and of the site (spine or three hip regions). The spine is preferable for diagnosis and for following treatment efficacy because of the large volume of trabecular bone. Ward's triangle is never used because of inferior precision *(5)*. Bone turnover is higher in trabecular than in cortical bone in osteoporosis. Generally, L1 through L4 vertebral bodies are evaluated. If degenerative changes occur in the spine, lumbar levels can be eliminated from evaluation as long as two vertebral bodies can be used. Once degenerative changes, scoliosis, compression fractures, or surgery have compromised the ability to accurately determine BMD or follow BMD, then the hip must be used for serial scans. The hip has significantly less trabecula then the spine and smaller regions of interest in the femoral neck and trochanter, so total hip must be used to follow BMD changes. Total hip density for follow-up has a large enough region of interest to minimize LSC. Because of the larger cortical bone component and slightly higher LSC compared to the spine, the changes in BMD take longer to identify in the hip. If the spine cannot be evaluated, both hips should be scanned. If only one hip is available for BMD, the hip and forearm should be scanned. The distal third of the forearm is used for evaluation.

LSC has been discussed earlier *(16)*. To determine whether BMD has significantly changed on follow-up scans, the LSC must be known. LSC should be established for the spine and hip, and should be reevaluated when a new scan operator is hired, a scanner is moved, hardware is changed, or significant software changes occur.

BMD scans and their evaluation can be affected by analysis and artifacts *(32)*. BMD is calculated by dividing BMC by area. Follow-up scans must have the same ROI placement and the same size area (within 2%) to ensure accurate comparison. Increased area lowers BMD falsely if BMC does not change and decreased area falsely increases BMD.

Artifacts from surgery (clips, screws, pumps, implants, navel jewelry, etc.) can increase BMD if it is over the spine or hip and lower BMD if it is over the soft-tissue ROI. Calcifications have the same effect. The calcifications may be vascular, posttraumatic, or heterotopic. Small artifacts can be removed on late-model scanners. Large artifacts usually preclude the scan site from analysis.

Changes in body weight also affect BMD. The analysis uses the soft tissue and bone attenuation of X-rays to determine BMD. If soft tissue changes significantly but BMC does not, then BMD based on X-ray attenuation is affected. If BMC also changes and weight changes, then comparison of follow-up scans is difficult because of multiple variables.

After all the issues of guaranteeing appropriate scans and follow-up BMD scans are ensured, the decision of how long to follow the patient is not well established. Generally, if the patient, if not on steroids, is followed every 2 yr until two consecutive scans are stable after the baseline scan is obtained, then the follow-up period can be lengthened. The interval between scans is also determined by the expected response to treatment based on knowledge of drug profile. If an increase in BMD is expected in 3 yr then follow up at 2 yr would be of benefit only if the BMD significantly decreased.

BMD is used for diagnosis initially and follow-up thereafter. An increase in BMD demonstrates efficacy of treatment. Stating no change in BMD means no bone loss or that further bone loss has been prevented. Some drugs may never increase BMD more than the LSC, but as long as BMD does not decrease it is presumed that the bone loss is prevented. A decrease in BMD indicates the possible need for adjunct treatment and evaluation for other causes of decreasing BMD.

BMD must be tracked on the same densitometer to follow treatment. Densitometers from different manufacturers use different X-ray sources, software, reference databases, and detectors, among other differences. Manufacturers state that the scan data can be transferred with appropriate data correction. However, pencil-beam scanners cannot be converted to fan-beam scan data. Depending on the versions of software between the scanners, conversion of data may not be accurate. In general, the best course of action when changing BMD scanners is to evaluate trends from previous scans and establish a new baseline on the new scanner.

Vertebral Fracture Assessment

Vertebral fracture assessment (VFA) has recently been approved for reimbursement. The importance of this assessment is the fact that a single vertebral fracture identified is predictive of a five times greater relative global fracture risk in the next year *(33,34)*. If two fractures are identified, the global fracture risk increases by 25 times over the next year. The identification of a fracture should alert the referring physician to consider a more aggressive approach to treatment. Fractures are identified using the semiquantitative method of Genant. Generally, the lateral thoracic and lumbar spine image allows for evaluation of T7 to L4, and in some patients the vertebral bodies are identified up to T4. The presence of a fracture and low bone density is a diagnosis of severe osteoporosis.

The semiquantitative technique has three grades and classifications of fracture. Grade 1, or mild, is approximately a 20 to 25% loss of height; grade 2 is a 25 to 40% loss of height, and grade 3 is more than a 40% loss of height. Loss of height can be an anterior wedge, biconcave (end plate), or crush. Vertebra plana can occur in osteoporotic patients but is uncommon. If vertebra plana is identified, a secondary cause of the fracture should be excluded.

The presence of disc degeneration, degenerative disease in the spine, and overlying bony anatomy may make the identification of a mild vertebral fracture difficult.

Indications for VFA include loss of height of more than 2 in. since age 21, treatment with steroids, and a previous history of transient unexplained back pain.

BMD Report

The BMD report (for any age patient) should include the patient's demographics, including age, sex, and race. Risk factors for low BMD and fracture

should be reported. Medications the patient is taking that affect BMD should be noted, along with the scan data, T-score where appropriate, Z-score, previous scan, comparison of scans, diagnosis, and fracture risk. Provide recommendations for a follow-up interval. Recommendations for treatment may be provided *(16)*. Vertebral fracture assessment is reported as a separate study because it has a different CPT code.

MRI and Micro-CT

Magnetic resonance imaging (MRI) is used to differentiate between pathological and osteoporotic fractures if necessary *(36)*. MRI is otherwise used as a research tool for evaluation of bone loss/osteoporosis at this time. Trabecular volume can be determined and three-dimensional architectural models can be reconstructed. Marrow signal is used to determine the number and connectivity of trabecula *(37–39)*. This information can be related to mechanical strength testing *(40)*. BMD cannot be determined by MRI. DXA BMD continues to remain the best predictor of fracture risk. Currently, the cost of MRI is prohibitive. In the future, combining the BMD and information from MRI may provide a better assessment of fracture risk and efficacy of treatment.

Micro-CT generally requires a sample of bone. High-resolution CT of the radius has been used in vivo to reconstruct trabecular architecture *(41,42)*. This fact makes the use of micro-CT a research tool, not practical for clinical use at this time. Micro-CT is excellent at reconstructing trabecular architecture. Generally, if a clinical specimen is analyzed the sample is taken from the iliac crest, a non-weight-bearing bone that rarely fractures in osteoporosis. Consequently, the analysis may indicate increased bone metabolism and architectural changes but does not relate to fracture risk. Micro-CT assessment of trabecula is associated with mechanical strength. Patterns of trabecular loss and architectural changes have not been associated with fracture risk.

Conclusion

DXA and QCT can be used to determine bone density in any age group. DXA is the gold standard. Quality assurance is necessary to provide accurate measurements. Reports are tailored to the individual, keeping in mind that WHO criteria are used for postmenopausal females. Z-scores are used for premenopausal females. Secondary causes of low bone density must be considered in premenopausal females with low bone density. Secondary causes of low bone density should also be considered in postmenopausal females. Loss of height and treatment with steroids are indications for VFA.

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