

Why Are QCT T-scores Usually Lower Than PA-DXA?

A Literature Review and Synopsis
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Original WHO “Guidelines” – Classification by T-Score

The World Health Organization (WHO) in 1994 issued a report on the relationship between certain measurements of bone mineral density (BMD) and the prospective risk of fractures ⁽¹⁾. In particular, the WHO evaluated BMD of the radius (forearm BMD) and found that for the population of patients where forearm BMD was approximately 2.5 standard deviations below the young normal mean or lower, the lifetime risk of sustaining an atraumatic, or osteoporotic, fracture, was high. Consequently, they classified this group of patients as “osteoporotic” based on the BMD value more than 2.5 SD below the young normal mean (T-score -2.5 or lower). This is not to say that all INDIVIDUAL patients in this group were at high risk of fracture, only that this cutoff level identified a POPULATION where the risk of fracture corresponded to the observed prospective fracture data. However, because BMD measurements alone did not uniquely separate fracture from non-fracture patients, it was not possible to use such a cutoff to determine the risk of fracture for the individual patient.

It is also well recognized that there are other risk factors for osteoporotic fracture beyond BMD, and that all these factors must be taken into account in the evaluation of the individual patient. For this reason, an additional classification was set up, “osteopenia,” with a T-score of -1 to -2.5. In essence, this classified the lower 15% of the young normal population as a group with some risk, with a higher and higher percentage falling into this category as the population aged, because of age-related and postmenopausal bone loss.

The WHO criteria were developed based on forearm BMD for postmenopausal, Caucasian women, and the authors of the report were careful to state that they should not be applied to other populations or other BMD measurement methodologies without further information. They were also careful to state that this classification is intended to be used only as one risk factor estimate in the evaluation of the patient’s overall lifetime risk for osteoporotic fracture.

The National Osteoporosis Foundation has adapted these guidelines to form its own recommendations for who should be considered for treatment based on BMD estimates and other factors. The NOF considers postmenopausal women with BMD T-score -1.5 or lower and at least one other risk factor (family history, adult fracture) as candidates for treatment, or any woman over age 65 with T-score -2 or lower ⁽²⁾.

Currently, there is substantial debate within the bone densitometry community about how to interpret BMD T-scores at different skeletal sites and using different methods. The International Society for Clinical Densitometry has recommended that when measuring peripheral skeletal sites (hand, forearm, heel), that a T-score of about -1 or lower (osteopenia) in a postmenopausal woman or someone else with risk factors is sufficient to recommend further work up, but that it is not sufficiently sensitive to be used to recommend treatment. If a T-score of a peripheral site is between -1 and -2, the recommendation is that a follow-up BMD of a central site (spine or hip) be done to confirm low BMD or determine that the patient may not need treatment ⁽³⁾.

The Health Care Financing Administration (HCFA/Medicare) recommends central BMD measurements (DXA or QCT of spine and/or hip) be done for confirming a possible diagnosis of osteoporosis by peripheral measurements, or as a baseline for patients starting therapy. No T-score values are given ⁽⁴⁾.

Updated WHO “Guidelines” – Restricted Use of T-Scores

Recently (2000), the Committee of Scientific Advisors, International Osteoporosis Foundation (the WHO committee) has issued a position paper updating the previous guidelines⁽⁵⁾. In large part this reevaluation was done because of the massive confusion caused by the previously-issued recommendations about using a T-score of -2.5 as diagnostic of osteoporosis. With the proliferation of methods for measurement and sites of measurement of BMD or other bone properties, a number of studies were done comparing these methods, and found that a T-score of -2.5 classified a widely varying percentage of patients as “osteoporotic” depending on the method used and the site measured. Given this disparity, the use of a T-score to “classify” a patient lost its meaning in clinical use. In the same patient population of elderly women, for example, between 19% and 66% of them were classified as “osteoporotic” depending on which skeletal site was measured with the same machine⁽⁶⁾.

The WHO committee updated recommendations⁽⁵⁾ for interpretation and use of BMD measurements can be summarized as follows:

1. Osteoporosis is defined based on the relationship between Total Hip BMD and hip fracture. A *diagnosis* of osteoporosis is made if Total Hip BMD T-score is -2.5 or lower. This definition identifies a 6% prevalence of osteoporosis for postmenopausal women age 60⁽⁷⁾. This definition also identifies only approximately 30% of women with spine fractures as osteoporotic⁽⁸⁾.
2. No other T-scores are used to make a diagnosis of osteoporosis.
3. BMD measurements at sites other than Total Hip can be used to evaluate relative risks for osteoporosis, and in conjunction with other risk factors are used to determine the need for intervention.
4. If a patient has low BMD by a measurement other than Total Hip, *and* has a fragility fracture, the patient should be considered osteoporotic.
5. *Intervention* thresholds using BMD or other assessments should *not* be based on *diagnostic* Total Hip T-score thresholds.

The practical clinical ramifications of these recommendations are that T-scores determined by most BMD methods or at most measurement sites are not to be used for a “diagnosis” of osteoporosis. However, clinicians should use BMD values, T-scores, Z-scores, or other parameters related to fracture risk in an overall assessment of the patient and in the decision whether or not to institute therapy. These recommendations are in general concordance with recommendations made by the National Osteoporosis Foundation, the European Foundation for Osteoporosis, and the International Society for Clinical Densitometry.

It is up to the clinician, in consultation with the practitioner making BMD measurements, to determine what guidelines should be used to determine intervention thresholds. It is recommended that T-scores alone should not be used to determine these guidelines, and in particular, that a T-score of -2.5 not be used to invoke intervention.

QCT and PA-DXA Spine T-scores

One of the most common questions asked by those who use QCT for BMD is why there is often a disparity between the spine QCT result and either a previous or subsequent spine PA-DXA result, with the QCT result invariably giving a lower T-score than the DXA result. A patient or a referring clinician has usually heard about the use of T-scores for DXA but not for QCT, and is concerned that QCT is classifying a patient as “osteoporotic” where the DXA result is “osteopenia” or even “normal”. Often concomitant with this is a question of why the PA-DXA of the spine and the DXA of the hip are also different, but this will not be addressed here because of the abundant literature on this subject.

As noted above, the most recent interpretation and updating of the WHO guidelines specifies that only the T-score for the Total Hip region of interest should be used as a means for “diagnosis” of osteoporosis. This is in contrast to the original guidelines, where the recommendations were based on forearm BMD and classified a much larger proportion of women as “osteoporotic” than does the current interpretation. Neither QCT nor PA-DXA of the spine were used to develop the WHO guidelines. However, clinicians have come to use the T-score as a convenient means of “classifying” a patient, even though that is not the intent of the guidelines. The following discussion is intended to explain some of the reasons that T-scores can be different between these two methods. This discussion is not intended to promote the use of a T-score classification scheme using either of these BMD methods.

There are four main reasons why spine T-scores by QCT can be different than T-scores by PA-DXA. Three of these are “technical” and one is “physiological” due to age-, hormone-, or treatment-related bone changes. Estimated magnitudes of these effects are given here, taken from published literature. These effects can be additive, that is, if more of one of them is present, one does not dominate but the total effect is the sum of those present.

1. Physiological effects of menopause and aging

Trabecular bone in the spine changes more rapidly after menopause or estrogen deficiency than any other region, including total spinal bone^(9,10). Because of this, more bone is lost as measured by QCT in the early years after menopause, but then this rate slows down after about age 60-65, while bone loss as measured by DXA in the spine, hip, or forearm occurs more gradually but continues well into the 70’s. This means that at any time early after menopause, the T-score as measured by QCT (or lateral spine DXA) will be more negative than that for PA-DXA of the spine, or for hip or forearm⁽⁷⁾. The hand and the heel lose at much slower rates, even slower than the hip, and T-scores for some methods such as heel ultrasound never even reach the -2.5 level on average for the population.

If the T-score for the mean BMD of the population reaches -2.5, this is equivalent to saying that one-half of the population is “osteoporotic,” that is, at high risk of fracture. This happens at about age 60-62 for QCT and lateral spine DXA, age 75 for PA spine DXA and forearm, and age 88 for hip⁽⁷⁾. This also means that for any given age, more patients will be classified as “osteoporotic” by QCT or lateral spine DXA than by the other methods.

While the fracture risk for any individual patient cannot be predicted from a BMD measurement, population risk estimates can be made to categorize a patient as low, moderate, or higher risk. The WHO T-score classification has attempted to do this based on the forearm BMD, but there are also other data to support this.

The lifetime risk for any osteoporotic fracture in white women age 50 years and older is 40%⁽¹¹⁾. At age 50, the fraction of women who have a low BMD (-2 SD or lower) at spine, hip, or forearm by DXA is 45%⁽¹¹⁾. At age 50, the fraction of women who have a low BMD (-2 SD or lower) at spine by QCT is 41%⁽¹²⁾. Thus, the published data show that QCT predicts lifetime fracture risk in populations the same as DXA.

The fact that QCT and DXA make the same predictions for lifetime fracture risk suggest that there are not so much differences in what the techniques measure, just in when each method can provide a BMD estimate in a patient that can be used to help assess the patient’s risk of fracture over the long term. The data suggest that QCT simply provides this assessment at an earlier age.

A simple table can show the relationship between QCT and DXA T-scores as a function of age for this physiological effect (from Reference 7).

| Mean T-scores for women as a function of age at various skeletal sites (ref 7) | | | | | |
|---|------------|----------------|---------------|----------------|------------------|
| Age | QCT | Lat-DXA | PA-DXA | Forearm | Total Hip |
| 50 | -1.4 | -1.3 | -0.8 | -0.8 | -0.5 |
| 55 | -1.9 | -1.7 | -1.1 | -1.0 | -0.7 |
| 60 | -2.5 | -2.2 | -1.4 | -1.3 | -1.0 |
| 65 | -2.9 | -2.6 | -1.8 | -1.7 | -1.2 |
| 70 | -3.2 | -3.4 | -2.1 | -2.1 | -1.5 |
| 75 | -3.5 | -4.2 | -2.2 | -2.5 | -1.7 |
| 80 | -3.6 | -5.1 | -2.6 | -3.5 | -1.9 |

2. Technical effects of osteophytes and aortic calcification

The structurally important bone in the spine is that of the cortex and trabecular regions of the vertebral body, which together take approximately 85% of the loads in the spine. In younger individuals, the trabecular bone takes about 80% of the load and the cortical shell 20%, while in osteoporotics, the total load bearing of the vertebra is reduced by about 60-70%, and the ratio is reversed so that the cortex takes about 70% of this remaining load because of the loss of all the trabecular bone ^(13,14).

In contrast to these contributions of cortical and trabecular bone to strength, extrasosseous calcification does not contribute to the structural strength of the spine, but because it is “mineral” it is included in any assessment of spine BMD where the whole spine is measured. The two primary components of extrasosseous calcification in the older female and male population are osteophytes and osteochondrosis (ligamentous or cartilage calcification) and deposits of calcium in the aorta and other blood vessels in the abdomen. When these are present, they can make up anywhere from 5-40% of the total “mineral” in the region of the lumbar spine assessed for BMD ⁽¹⁵⁾.

PA-DXA of the spine estimates the amount of all mineral in the path of the x-ray beam, while QCT estimates only the trabecular bone density within the vertebral body. Because osteophytes are usually quite dense relative to the vertebra, including them in the analysis raises the average BMD of any vertebra or vertebral segment which includes them. Several studies have been done to estimate this effect quantitatively. A typical example compares osteophyte “grade” with the effect on measured BMD. The following table is derived from data in reference 16 for a postmenopausal non-fracture population average age 62 years old.

| Effect of osteophytes on spine T-score by QCT or PA-DXA (ref 16) | | | |
|---|----------------|-------------------|-----------------------|
| Osteophyte Grade | QCT BMD | PA-DXA BMD | T-score effect |
| 0 | 112 | 0.82 | 0 |
| 1 | 113 | 0.89 | +0.6 |
| 2 | 100 | 0.95 | +1.1 |
| 3 | 114 | 1.10 | +2.3 |

The osteophytes had no significant effect on the measured QCT BMD values in this study.

Other authors have found the presence of various degenerative factors to increase from 35% of postmenopausal women age 55 up to 80% of women at age 70⁽¹⁷⁾. These authors have recommended that interpretation of PA-DXA spine measurements for women at or above this age range should be complemented by plain film radiographs in order to assess the effect of degenerative changes. Similar recommendations have been made by others, even to the point that PA-DXA of the spine should not even be done in the over-65 population unless hypertrophic changes have been excluded^(18, 19).

3. Technical effects due to increased Body Mass Index

Many studies have shown that increased body mass index, that is, obesity versus normal body habitus, cause PA-DXA spine BMD values to be high. This has been attributed by some researchers to physiological factors (increased body weight causing increased mechanical forces on bone, or more body fat increasing circulating estrogen levels), but anomalous clinical results have cast doubt on such theories⁽²⁰⁾. The latter study showed BMD increases by DXA of 0.8 T-score in heavy osteoporotics (BMI>26 kg/m²) compared to normal (BMI<25 kg/m²). Recent studies have attributed the increased BMD by DXA to errors in the DXA measurement itself⁽²¹⁻²³⁾.

A direct comparison between QCT and DXA⁽²³⁾ showed that for postmenopausal patients classified as clinically obese (Body Mass Index > 27 kg/m² as defined by the American Society of Clinical Nutrition), the average T-score by PA-DXA was 1.45 units higher in obese patients than in age and height matched controls, while the QCT T-scores did not differ between the groups. This study was done using Hologic QDR bone densitometers, so it must be qualified. However, other researchers have shown similar effects with different systems⁽²²⁾.

4. Technical effects due to bone size

PA-DXA estimates bone mineral content in a projected area, then BMD is calculated by dividing the BMC by the area. Because the bones in the spine and hip generally scale in 3 dimensions, the “thickness” of large bones along the projected measurement is greater than for smaller bones, so the total bone mineral content increases faster than the projected area. This causes PA-DXA BMD estimates to be higher for large-stature patients than for smaller individuals, even if the volumetric BMD is the same. Researchers using DXA have tried to estimate and correct for this effect by measuring the spine both from PA and lateral directions and estimating the “volume” of the vertebra, then scaling the BMD value to a “normal” bone size if either tall or petite patients are measured (or children). However, this is not done in clinical practice, and normative data provided with DXA systems does not take into account patient height or estimated bone size in the clinical comparison.

With QCT there is no evidence for a relationship across populations of bone size on the BMD result. Within a given patient, BMD decreases slightly moving down the lumbar spine⁽²⁴⁾, in contrast to the increase in area BMD as measured by DXA⁽²⁵⁾. The effect of bone size on the T-score for DXA measurements can be estimated based on the relationship between patient height and bone size, but differs for different DXA manufacturers, so it is difficult to quantify; however, recent studies have addressed this effect in children so it may be possible to estimate the effects. In addition, “volumetric” DXA estimates made by using both PA and lateral DXA data have been used to try to correct for this effect, but have not improved the diagnostic sensitivity for osteoporosis.

Summary

The reason for observed differences between QCT and PA-DXA T-scores in individual patients may be multiple, but will generally fall into one or more of 4 categories. Forearm data given for comparison.

1. Age and postmenopausal status: mean T-scores for QCT and PA-DXA

| Age | 50 | 55 | 60 | 65 | 70 | 75 | 80 |
|---------|------|------|------|------|------|------|------|
| Forearm | -0.8 | -1.0 | -1.3 | -1.7 | -2.1 | -2.5 | -3.5 |
| QCT | -1.4 | -1.9 | -2.5 | -2.9 | -3.2 | -3.5 | -3.6 |
| PA-DXA | -0.8 | -1.1 | -1.4 | -1.8 | -2.1 | -2.2 | -2.6 |

2. Osteophytes and other extravertebral calcification

QCT has no effect of osteophyte grade on T-score

| PA-DXA | | | | |
|-------------------|---|------|------|------|
| Grade | 0 | 1 | 2 | 3 |
| Change in T-score | 0 | +0.6 | +1.1 | +2.3 |

3. Body Mass Index (obesity)

BMI > 27 kg/m², PA-DXA T-score elevated by 1.45 T-score units over QCT.

BMI > 27 kg/m² corresponds roughly to a woman 5'2", 150 lbs, or 5'7", 175 lbs.

4. Body Stature (height)

No quantitative data, but generally tall patients will have a higher areal BMD (more positive T-score) than expected, and short patients will have a lower areal BMD (more negative T-score) than expected.

References

1. World Health Organization 1994. Assessment of fracture risk and its application to screening for postmenopausal osteoporosis. Technical Report Series, WHO, Geneva.
2. National Osteoporosis Foundation. 1998. Guidelines for the use of bone densitometry. National Osteoporosis Foundation, Washington DC.
3. Miller PD, Bonnick SL, Johnston CC Jr, Kleerekoper M, Lindsay RL, Sherwood LM, Siris ES. 1998. The challenges of peripheral bone density testing: Which patients need additional central density skeletal measurements? *J Clin Densitom* 1: 211-217.
4. HCFA Bone Mass Measurement Guidelines, [HCFA-3004-IFC], RIN 0938-AI89, Federal Register June 24, 1998, 63(121): 34320-34328.
5. Kanis JA, Gluer C-C. 2000. An update on the diagnosis and assessment of osteoporosis with densitometry. *Osteoporosis Int* 11: 192-202.
6. Greenspan SL, Maitland-Ramsey L, Myers E. 1996. Classification of osteoporosis in the elderly is dependent on site-specific analysis. *Calcif Tissue Int* 58: 409-414.
7. Faulkner KG, von Stetten E, Miller P. 1999. Discordance in patient classification using T-scores. *J Clin Densitom* 2: 343-350.
8. Kroger H, Lunt M, Reeve J, Dequeker J, Adams JE, Birkanhager JC, et al. 1999. Bone density reduction in various measurement sites in men and women with osteoporotic fractures of spine and hip. The European Quantitation of Osteoporosis Study. *Calcif Tiss Int* 64: 191-199.
9. Ettinger B, Genant HK, Cann CE. 1985. Long-term estrogen replacement therapy prevents bone loss and fractures. *Ann Intern Med* 102:319-324.
10. Prior JC, Vigna YM, Wark JD, Eyre DR, Lentle BC, Li DKB, Ebeling PR, Atley L. 1997. Premenopausal ovariectomy-related bone loss: A randomized, double-blind, one-year trial of conjugated estrogen or medroxyprogesterone acetate. *J Bone Miner Res* 12: 1851-1863.
11. Melton LJ, III, Chrischilles EA, Cooper C, Lane AW, Riggs BL. 1992. Perspective: How many women have osteoporosis? *J Bone Miner Res* 7: 1005-1010.
12. Cann CE, Genant HK, Kolb FO, Ettinger B. 1985. Quantitative computed tomography for prediction of vertebral fracture risk. *Bone* 6: 1-7.
13. Rockoff SD, Sweet E, Bluestein J. 1969. The relative contributions of trabecular and cortical bone to the strength of human lumbar vertebrae. *Calcif Tissue Res* 3: 163-173.
14. Faulkner KG, Cann CE, Hasegawa BH. 1991. Effect of bone distribution on vertebral strength: Assessment with patient-specific nonlinear finite element analysis. *Radiology* 179: 669-674.
15. Cann CE, Rutt BK, Genant HK. 1983. Effect of extraosseous calcification on vertebral mineral measurement. *Calcif Tissue Int* 35: 647.
16. Yu W, Glueer CC, Fuerst T, Grampp S, Li J, Lu Y, Genant HK. 1995. Influence of degenerative joint disease on spinal bone mineral measurements in postmenopausal women. *Calcif Tissue Int* 57: 169-174.
17. Rand Th, Seidl G, Kainberger F, Resch A, Hittmair K, Schneider B, Glueer CC, Imhof H. 1997. Impact of spinal degenerative changes on the evaluation of bone mineral density with dual energy x-ray absorptiometry (DXA). *Calcif Tissue Int* 60: 430-433.
18. Baran DT, Faulkner KG, Genant HK, Miller PD, Pacifici R. 1997. Diagnosis and management of osteoporosis: Guidelines for the utilization of bone densitometry. *Calcif Tissue Int* 61: 433-440.

19. Liu G, Peacock M, Eliam O, Dorulla G, Braunstein E, Johnston CC. 1997. Effect of osteoarthritis in the lumbar spine and hip on bone mineral density and diagnosis of osteoporosis in elderly men and women. *Osteoporosis Int* 7: 564-569.
20. Shiraki M, Shiraki Y, Aoki C. 1999. High prevalence of vertebral fracture, low serum osteocalcin and high mortality in osteoporotics with over weight. *J Bone Miner Res* 14: S520.
21. Formica C, Loro ML, Gilsanz V, Seeman E. 1995. Inhomogeneity in body fat distribution may result in inaccuracy in the measurement of vertebral bone mass. *J Bone Miner Res* 10: 1504-1511.
22. Totill P, Avenell A, Reid DM. 1994. Precision and accuracy of measurements of whole body bone mineral: Comparison between Hologic, Lunar, and Norland dual energy x-ray absorptiometers. *Br J Radiol* 67: 1210-1217.
23. Weigert JM, Cann CE. 1999. Dual energy x-ray absorptiometry (DXA) in obese patients: Are normal values really normal? *J Women's Imaging* 1: 11-17.
24. Steiger P, Block JE, Steiger S, Heuck AF, Friedlander A, Ettinger B, Harris ST, Glueer CC, Genant HK. 1990. Spinal bone mineral density measured with quantitative CT: Effect of region of interest, vertebral level, and technique. *Radiology* 175: 537-543.
25. Kleerekoper M. 1999. Bone density reference data, Appendix VI. In Favus MJ (ed). *Primer on the Metabolic Bone Diseases and Disorders of Mineral Metabolism*, Lippincott Williams and Williams, Philadelphia, pp. 483-484.

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