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Original article

Bone mineral density in vertebral compression fractures

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SUMMARY. *Objective*. To estimate the best cut-off point of bone mineral density (BMD) measured simultaneously by dual X-ray absorptiometry (DEXA) and quantitative computed tomography (QCT) to rule out vertebral compression fractures and determine the prognosis. *Material and methods*. Twelve females with vertebral fractures and 27 with no fractures were included. BMD was measured in both groups by DEXA and QCT. *Results*. In women with fractures, DEXA and QCT matched in classifying 9 patients with severe osteoporosis but with very different BMD averages (p = 0.0001). The other 3 were classified as osteopenic by DEXA and as severely osteoporotic by QCT (p = 0.0001). Of the 27 patients with no fractures, 21 were considered as normal; of the remaining 6 patients, one was classified by DEXA as normal while QCT classified her as having osteopenia; and 5 patients were considered by DEXA as osteopenic while QCT classified them as osteoporotic (p = 0.0001). The best cut-off point to simultaneously improve the sensitivity and specificity of DEXA and QCT, according to the ROC curves, would be 0.7705 and 0.6515 g/cm^2, respectively. When applied in parallel, these values increased the sensitivity from 83.3% to 91.7% in detecting women at high risk of vertebral compression fracture, compatible with bone brittleness. *Conclusions*. 1. When the purpose is to discriminate and predict the presence or absence of fracture risk, the case classification (normal, osteopenic, osteoporotic, or se-

RESUMEN. *Objetivo.* Estimar los mejores puntos de corte de la densidad mineral ósea (DMO), medida simultáneamente por absorciometría dual de energía de rayos X (DEXA) y tomografía computada cuantitativa (TCC), para discriminar y pronosticar fractura por compresión de cuerpos vertebrales. *Material y métodos*. Se incluyeron 12 mujeres con fractura de cuerpos vertebrales y 27 sin fractura. En ambos grupos se midió DMO por DEXA y TCC. *Resultados.* En las fracturadas DEXA y TCC concordaron en clasificar con osteoporosis severa a 9 pacientes, pero con promedios de DMO muy diferentes (p = 0.0001); las 3 restantes, DEXA las clasificó con osteopenia y TCC con osteoporosis severa (p = 0.0001). En las no fracturadas se concordó en 21 casos, todos considerados normales; en las 6 restantes: DEXA clasificó 1 como normal, mientras TCC con osteopenia. En los otros 5, DEXA los clasificó con osteopenia mientras TCC con osteoporosis (p = 0.0001). Los mejores puntos de corte para elevar simultáneamente la sensibilidad y especificidad de DEXA y TCC, según las curvas COR, serían: 0.7005 y 0.6515 g/cm^2 respectivamente; que aplicados en paralelo incrementan la sensibilidad de 83.3% a un 91.7% para detectar a las mujeres con alto riesgo de fractura por compresión de cuerpos vertebrales, compatibles con fragilidad ósea. *Conclusiones.* 1. Para fines de discriminar y predecir riesgo o no riesgo de fractura, la clasificación de los casos (normales, osteopénicos, osteoporóticos u osteoporóticos severos) según los T Score de la DMO medida por DEXA, no

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verely osteoporotic) based on the BMD T-Score measured by DEXA does not accurately match the middle BMD levels of the vertebral bodies in our sample. 2. We recommend using both diagnostic procedures. While one measures the cortical BMD the other measures the trabecular BMD. Together, both are capable of more accurately classifying cases to predict the risk of vertebral compression fracture.

Key words: fractures, bone mineral density, dual X-ray absorptiometry, computed tomography.

se ajusta exactamente a los niveles medios de DMO de los cuerpos vertebrales de nuestra muestra. 2. Conviene utilizar ambos procedimientos diagnósticos pues mientras uno mide la DMO cortical otro mide la DMO trabecular y, entre ambos, clasifican mucho mejor los casos con fines de predecir el riesgo de fractura por compresión de cuerpos vertebrales.

Palabras clave: fracturas, densidad mineral ósea, absorciometría dual de energía de Rx, tomografía computada.

Introduction

Setting the bone mineral density (BMD) limits that allow estimating the risk of vertebral compression fracture is not a minor problem[1-5] for various reasons. 1. Previous studies report that the incidence and prevalence of low BMD-related vertebral fractures in post-menopausal women has increased since the 1980s. 2. After a first vertebral compression fracture, the risk of a second one, either at the level of the spine itself or in other bones, especially the hip, increases. 3. The mortality rate of women during the year following a first fracture is 20% higher than that of women without a fracture; together with the major disability caused by these fractures, the treatment of fractures and their sequelae has become a major economic burden that is growing. 4. After the 1993 consensus, reviewed in 1997, osteoporosis was defined as "a systemic disease characterized by a bone compromise predisposing people to increased risk of fractures. The outcomes are due to a reduced bone capacity to bear the torsion and compression stresses".[6] WHO has added to this definition a statement explaining that fractures due to bone brittleness are those caused by a damage that is not severe enough to break a normal bone. Clinically, a fracture due to bone brittleness may be defined as one resulting from minimum trauma, a high or low fall or even from unidentified trauma.

Currently the BMD measurement with dual energy X-ray absorptiometry (DEXA) is considered as the most sensitive and specific means to diagnose osteoporosis. However, DEXA basically measures cortical BMD, which may underestimate the true trabecular BMD levels. Delimitation is very significant in this paper since it is known that bone mass in vertebral bodies is composed of 20% cortical bone and 80% trabecular bone. In contrast, quantitative computed tomography basically measures trabecular bone mass. The discriminating power of QCT to classify subjects with or without vertebral compression fractures has been shown since the mid 1980s[1] by accurate measurements of trabecular BMD. However, there are no current studies to accurately determine the discriminating power of both diagnostic means when used in parallel or in combination to rule out vertebral fractures.[7]

The following concern prompted this study: to determine whether the bone mineral density (BMD) measurement through quantitative computed tomography, in combination or in parallel with dual energy X-ray absorptiometry, can increase the discriminating power to distinguish vertebral bodies with and without compression fractures in Mexican mestizo women over 40 years of age. We also inferred that the study could provide the best BMD cut-off points to estimate the future chance of a woman with the already mentioned characteristics of being classified in the vertebral "fracture" or "non fracture" group. On the other hand, when BMD is measured either with DEXA or with QCT, Mexican mestizo women are classified as normal, osteopenic, osteoporotic, or severely osteoporotic, depending on the number of standard deviations the measured BMD is away from the mean BMD established by WHO, according to the reference group.[8] However, the fact that the worldwide reference group used by WHO was made up of Caucasian women has led to a silent debate around the external validity of such a reference group,[9] i.e., around the global generalization of its data.

We are asking the following question: is a determined BMD value in a Mexican mestizo woman equivalent to a certain level of the osteoporosis classification based on our own standards? We believe the question is valid if we trust the current WHO definition of osteoporosis concerning the crucial concept of risk of bone brittleness-related fracture. For instance, a woman over 40 years of age, with a BMD of 0.7000 g/cm^2 as measured by DEXA may be classified as "normal" because it is -1.0 standard deviations away from the mean BMD of the reference group used by WHO. However, how are we to classify her based on the mean BMD of Mexican mestizo women used as internal reference? The answer may be obtained by starting with the BMD cut-off point to first discriminate between women with and without fractures due to compression of the verte-

bral body or bone brittleness. This statement is reinforced by studies such as those by Melton[9] and Kanis[10] who felt that "every woman with a bone brittleness vertebral fracture … must be considered at high risk regardless of whether or not the BMD is within the ranges of osteoporosis". Obviously these are the osteoporosis ranges based on the WHO reference group. Whether the combination of quantitative methods may increase the diagnostic accuracy and estimate the fracture risk is still debatable. One possible combination might be DEXA with QCT except that according to the systematic review quoted by Brown et al,[6] the studies reported about the use of QCT have yet to meet the criteria of level 1 evidence. These criteria are as follows.

I. Independent interpretation of the testing results evaluated
II. Independent interpretation of the diagnosis made under the gold standard
III. Screening patients with suspected disease without actual confirmation
IV. Reproducibility of the test being evaluated and the gold standard
V. Including at least 50 people with the disease and 50 people without the disease

Items at evidence level 2 are considered those meeting 4 criteria in level 1. Level 3 meet 3 of those criteria; and level 4 meet 1 or 2 criteria in level 1.

In summary, this study was developed to show the following: 1) an anticipated classification with explicit criteria of a group of Mexican mestizo women over 40 years of age as a) with compression fracture; and b) without vertebral compression fracture, and the combined or parallel use of DEXA and QCT to measure BMD, would allow us to improve the discriminating power to distinguish both groups and estimate the a posteriori chance that a woman over 40 years of age has to be classified in either group, based on her BMD. 2) The best cut-off point for BMD to discriminate patients with or without fracture might redefine the WHO classification in our setting based on the bone brittleness-related vertebral body fracture concept.

Material and methods

In the clinical and radiological study, 39 patients over 40 years of age were included. Of them, 12 had vertebral compression fracture due to minimum or no trauma (compatible with bone a brittleness fracture) and 27 patients had no fractures or a history of fracture of those bones. BMD in both groups was measured by DEXA and QCT simultaneously.

Before the final measurements, the variation coefficients in both diagnostic procedures were assessed in a pilot group of 20 women (10 with fractures and 10 without vertebral body fractures). The coefficients were found to be less than 2%. The equipment was calibrated after these evaluations and the same person, an expert in imaging, performed the final measurements by DEXA and QCT, which were interpreted by two independent observers. The diagnosis of fracture was based on the radiological criteria pointed out in the systematic review by Brown et al.[6] and confirmed also by two additional independent evaluators.

Data were entered and processed using SPSS 11.0 for Windows. The mean ages and BMD were calculated by means of the General Linear Model for the single univariance analysis, with both groups (fracture and non fracture) and the WHO classification, based on the T Score (normal, osteopenia, osteoporosis, or severe osteoporosis) as fixed factors. The discriminating analysis was made to contrast the usefulness of BMD measurements to determine the chance of women of being classified into either study group. Finally, the ROC curves allowed estimating the sensitivity and specificity of both procedures using the best BMD cut-off points for the sample.

Results

Table 1 shows that out of the 12 patients considered as having fractures according to the WHO criteria, 3 patients were classified as osteopenic based on the cortical BMD measured by DEXA. In contrast, the same patients were classified as having severe osteoporosis based on the trabecular BMD measured by QCT. In the remaining 9 patients the DEXA and QCT classifications matched as severe osteoporosis. However, in both situations the mean BMD according to DEXA vs. QCT was significantly different ($p = 0.0001$ respectively). Notice that the mean BMD measured by DEXA was systematically above the QCT measurement.

Table 2 shows that DEXA and QCT matched in classifying 7 women with no fractures as having osteopenia. However, while according to DEXA 5 women or more were classified as having osteopenia, according to QCT the same women were classified as having osteoporosis. Regarding the second item in *Table 2* DEXA and QCT matched in classifying 2 women as having osteoporosis. Finally both diagnostic procedures classified 12 controls as normal, but the last control was classified as normal by DEXA while QCT classified her as having osteopenia.

Figure 1 shows the intersection of simultaneous BMD values obtained with DEXA and QCT (Pearson's r correlation coefficient between DEXA and QCT in women both with and without fractures is 0.98, $p = 0.0001$) allowing women to be divided into two different groups: with and without fractures. However, the dispersion cloud also shows that in some patients with no fractures the BMD crossed values overlap with those of women with fractures. This shows the need for a different classification procedure such as the discriminating analysis and, of course, the ROC curves, to estimate the best cut-off points simultaneously thus increasing the sensitivity and specificity of measurements.

Table 1. Mean BMD (g/cm²) in women with fractures (n = 12).

WHO/DEXA	WHO/QCT	DEXA/ Cortical BMD	QCT/ Trabecular BMD	Age	N
Osteopenia	Severe Osteoporosis	0.7436	0.6466	54	3
Severe osteoporosis	Severe Osteoporosis	0.5905	0.5277	60	9
Total		0.6188	0.5570	58	12

Table 2. Mean BMD (g/cm²) in women with no fractures (n = 27).

WHO/DEXA	WHO/QCT	DEXA/ Cortical BMD	QCT/ Trabecular BMD	Age	N
Osteopenia	Osteopenia	0.7821	0.7240	61	7
	Osteoporosis	0.7080	0.6470	68	5
Osteoporosis	Osteoporosis	0.6755	0.6115	60	2
Normal	Normal	0.8184	0.8185	63	12
	Osteopenia	0.8900	0.8910	48	1
Total		0.8074	0.7463	63	27

Table 3. Classification of women with or without fractures according to the discriminating analysis /BMD and WHO classification.

Panel A. Discriminating analysis by BMD and WHO Classification for DEXA

	Prediction		
Original	With fracture	Without fracture	
With fracture	9	3	12
Without fracture	2	25	27
Total	11	28	39
82.1% properly classified			

Panel B. Discriminating analysis by BMD and WHO classification for QCT

	Prediction		
Original	With fracture	Without fracture	
With fracture	12	0	12
Without fracture	7	20	27
Total	19	20	39
87.2% properly classified			

According to the tables shown, and following the WHO classification and the trabecular BMD measured by QCT, 7 controls (26%) would be classified as patients with osteoporosis and therefore at high risk for vertebral compression fracture. On the other hand, according to the cortical BMD only 2 controls (7.4%) would have BMD levels consistent with those in patients with fractures. Considering only the BMD levels and the corresponding WHO classification, the discriminating analysis clearly confirms this as seen on panels A and B of *Table 3*.

Now, if age is considered as an independent factor together with the BMD level measured by DEXA or by QCT, the discriminating analysis points out that as much as 92.3% of the original cases (with and without fractures) would be properly classified, as seen on panels A and B of *Table 4*.

Notice now that according to the discriminating analysis, 100% (n = 12) of the women with fractures would be properly classified in terms of BMD by DEXA and QCT depending on the age of patients. However, 3 of the 27 women without fractures might be classified on a predictive basis as women with fractures. In other words, as much as 11.1% of them would be at risk of imminent fracture. BMD levels in these 3 cases were those shown on *Table 5*.

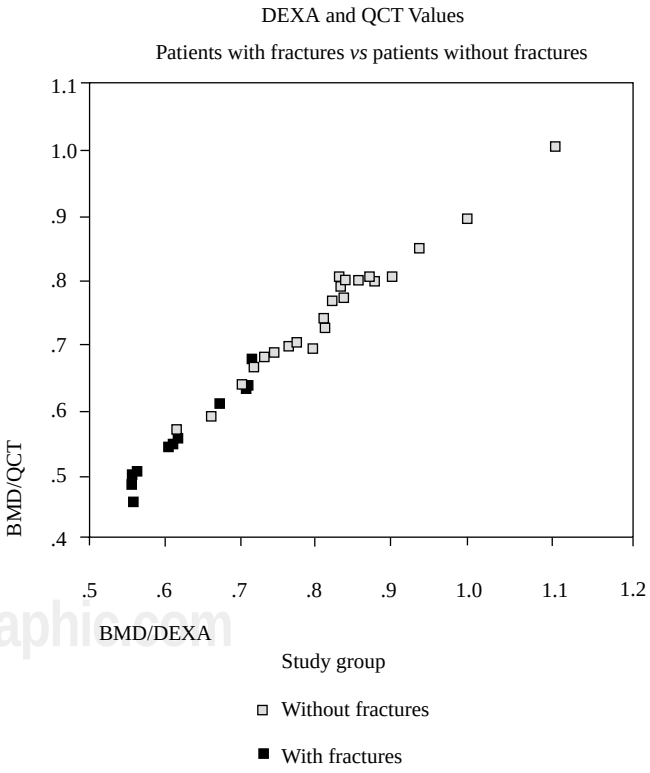

Figure 1. Dispersion diagram for DEXA and QCT by study group.

Table 4. Classification of women with or without fractures by the discriminating analysis: BMD and age.

Panel A. BMD Discriminating classification by DEXA and age

	Prediction		
Originals	With fracture	Without fracture	
Fracture	12	0	12
Without fracture	3	24	27
Total	15	24	39

92.3% properly classified

Panel B. Discriminating classification by BMD, by QCT and age

	Prediction		
Originals	With fracture	Without fracture	
Fracture	12	0	12
Without fracture	3	24	27
Total	15	24	39

92.3% properly classified

Table 5. Patients without fractures that might be classified on a predictive basis as having a fracture (risk for fracture).

Case	BMD/DEXA	BMD/QCT	Age
1	0.610	0.565	
	Osteopenia	Osteoporosis	72
2	0.656	0.585	
	Osteoporosis	Osteoporosis	50
3	0.695	0.638	
	Osteoporosis	Osteoporosis	70

Table 6. Patients with no fractures classified as having osteopenia by DEXA and osteoporosis by QCT.

Case	BMD/DEXA	BMD/QCT	Age
4	0.700	0.630	
	Osteopenia	Osteoporosis	78
5	0.710	0.665	
	Osteopenia	Osteoporosis	75
6	0.735	0.685	
	Osteopenia	Osteoporosis	66
7	0.785	0.690	
	Osteopenia	Osteoporosis	50

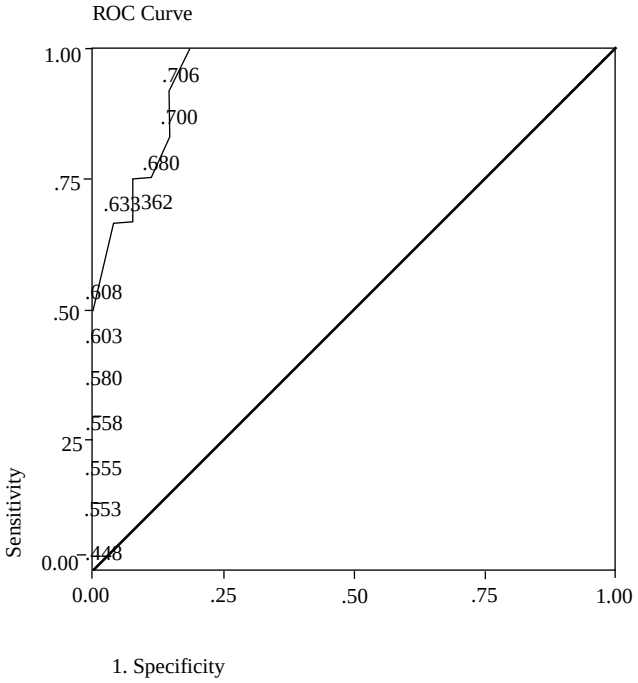

Figure 2. ROC Curve for the BMD estimated by DEXA.

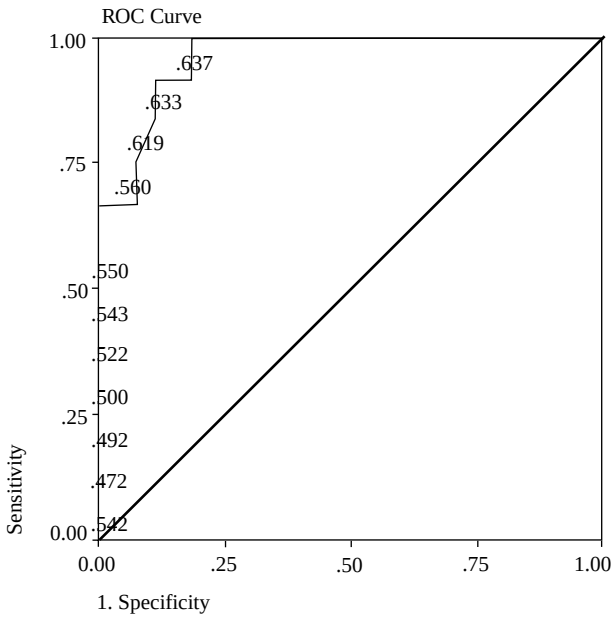

Figure 3. ROC Curve for the BMD estimated by QCT.

These cases are part of the 7 cases presented in *Table 3* Panel B, which were classified with osteopenia by DEXA and osteoporosis by QCT. BMD levels of the other 4 cases were those shown in *Table 6*.

In the least bad scenario DEXA would underestimate 4 cases with a high chance of fracture, and in the worst case scenario it would be actually underestimating 7 women who, according to QCT, would be susceptible to fracture due to their low trabecular BMD levels. ROC curves for both measures are as follows.

The first ROC curve *(Figure 2)* corresponds to the cut-off points for the BMD estimated by DEXA (area under the curve 0.954, p = 0.0001) where 0.7005 g/cm^2 BMD would have a sensitivity of 83.3% with 14.8% false positives. In fact, notice that all 3 cases pointed out in *Table 5* are within the above cut-off point and, at the same time, they were classified as osteopenia. On the other hand, the remaining 9 patients had a mean 0.5905 g/cm^2 of BMD and were classified as having severe osteoporosis. In the next ROC curve *(Figure 3)*, that represents the BMD by QCT (area

under the curve 0.961, p = 0.0001), a 0.6515 g/cm^2 result would show a 91.7% sensitivity with 14.8% false positives, and all patients (17 = 12 with fractures + 5 without fractures) who were classified as having osteoporosis by QCT were under the cut-off point. Of these, at least 8 were classified as osteopenia by DEXA (3 with fractures and 5 without fractures).

Finally, taking as reference the cut-off points of 0.7005 g/cm^2 for DEXA and 0.6515 gcm^2 for QCT, again the sensitivity of the former would be in the order of 83.3% (probability ratio 17.4, p = 0.0001) and 91.7% for QCT (probability ratio of 17.6, p = 0.0001). Likewise, it is possible to estimate that the approximate relative risk would be 28.7 (95% CL: 4.5-183.3) plus the probability of patients with fractures (compared to patients without fractures) to be within or under the 0.7005 g/cm^2 BMD measured by DEXA. The approximate relative risk would increase to 63.2 (95% CL: 6.3 – 634.7) plus the probability of patients with fractures (compared to patients without fractures) to be within or under the 0.6515 g/cm^2 BMD measured by QCT.

Discussion

Until the time when this research work was closed, it clearly appeared that it could be classified as evidence level 2 in accordance with the criteria proposed by Brown et al.[6] We met 4 of the 5 criteria specified by these authors. However, it was not possible to gather at least 50 women with fractures and 50 women without fractures. In spite of this, the first results clearly indicate that DEXA and QCT may become combined parallel tests to predict the risk of vertebral compression fractures due to bone brittleness. In fact, according to the systematic review by Brown et al, every patient who sustained a vertebral compression fracture should be classified as high risk for fractures elsewhere, regardless of whether or not the BMD is within the osteoporosis range according to the WHO T Score. Obviously the 12 patients with fractures should be considered at high risk for further vertebral fractures or fractures elsewhere, especially the hip,[7-9] due to bone brittleness.

If we trusted only the DEXA results, 3 (25%) of the above 12 patients would be classified as having osteopenia; on the other hand, if subject to QCT, these same 12 women (100%) would be classified as having severe osteoporosis. The results better match the patient definition of high risk for fracture. This classification further predicts the discriminating analysis.

The main problem would be classifying all 27 women acting as controls. According to DEXA, 13 patients (48.1%) would be truly normal. Of these, according to the QCT measurement, 11 (44.4%) would actually be normal. In summary, in terms of specificity, both procedures would be very similar; nonetheless, in terms of sensitivity, DEXA would underestimate the risk for a probable fracture in 6 control women, especially because the mean age of these women is 68 years. According to QCT, these women would be considered as borderline with overt osteoporosis because of their trabecular BMD. In other words, QCT would point out that 6/27 (22.2%) control women are actually at high risk for a probable vertebral body fracture. This result is similar to the one predicted in the tables presented by Kanis et al,[10] in which a 70 year old Caucasian woman and a T-score classified as -2.5 standard deviations would involve a 16.2% chance of sustaining a fracture due to bone brittleness at the hip level.

The reason to use DEXA combined or in parallel with QCT is based on studies describing the pathological microanatomy of bone brittleness in vertebral bodies. According to Aaron et al.[11] and Seeman[12] the loss of connectivity in trabecular basic multicellular units (BMU) prevails in elderly women. Structural failure occurs when the bone remodeling process in periosteal bone formation (which is also decreased) is unable to compensate for most of the endosteal BMD and trabecular loss and ultimately microlesions and perforations occur, and the bone architecture is destroyed when the vertebral body brittleness falls below the fracture threshold.

We drew at least the following conclusions: 1) Cases are classified according to the BMD T Score measured by DEXA as normal, with osteopenia, with osteoporosis, or with severe osteoporosis. This classification does not accurately match the mean BMD levels in vertebral bodies in our series to discriminate and predict the presence or absence of fracture risk. 2) It would be desirable to use both diagnostic procedures. While DEXA measures cortical BMD, QCT measures trabecular BMD and together, both may provide a better patient classification that allows predicting the risk of vertebral body compression fractures. In fact, the best BMD cut-off points to predict the risk for a vertebral compression fracture would be $\leq$0.7005 g/cm^2 for the cortical BMD measured by DEXA, and $\leq$0.6515 g/cm^2 for the trabecular BMD measured by QCT.

Bibliography

1. Cann CE, Genant HK, Kolb FO, Ettinger B: Quantitative computed tomography for prediction of vertebral fracture risk. *Bone* 1985; 6(1): 1-7.
2. Cooper C: Osteoporosis an epidemiological perspective: a review. *J R Soc Med* 1989; 82(12): 752-57.
3. Guidelines for preclinical evaluation and clinical trials in osteoporosis. Geneva: WHO 1999: 59.
4. Harma M, Heliovaava M, Aromaa A, Kneckt P: Thoracic spine compression fractures in Finland. *Clin Orthop* 1986; (205): 189-94.
5. Heaney RP: Qualitative factors in osteporotic fracture: the state of the question. In: Christiansen C, et al., eds. Osteoporosis 1987, 1. Proceedings of the international symposium on osteoporosis, Denmark, 1987. Copenhagen, Osteopress ApS, 1987: 288-7.
6. Brown JR, Josse RG: 2002 clinical practice guideline for diagnosis and management of osteoporosis in Canada. *CMAJ* 2002; 12: 167: S1-S34.
7. Klotzbuecher CM, Ross PD, Landsman P, Abbott TA, Berger M: Patients with prior fractures have an increased risk of future frac-

tures: a summary of the literature and statistical synthesis. *J Bone Miner Res* 2000; 15(4): 721-39.
8. McClung MR, Geusens P, Miller PD, Zippel H, Bensen WG, Roux C, et al : Effects of risendronate on the risk of hip fracture in elderly women. *N Engl J Med* 2001; 344(5): 333-40.
9. Melton LJ 3rd, et al: Vertebral fractures predict subsequent fractures. *Osteoporos Int* 1999; 14(10): 214-21.
10. Kanis JA, et al: Ten year probabilities of osteoporotic fractures according to BMD and diagnostic thresholds. *Osteoporos Int* 2001; 12(12): 989-95.
11. Aaron JE, Makins NB, Sagreiya K: The microanatomy of trabecular bone loss in normal aging men and women. *Clin Orthop* 1987; (215): 260-71.
12. Seeman E: Pathogenesis of bone fragility in women and men. *Lancet* 2002; 359(9320): 1841-50.