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Research Article

Bone Mineral Density as Risk Factor for Bone Fractures

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Received: July 18, 2017; **Published:** August 04, 2017

Abstract

Osteoporosis is characterized by low bone mineral density (BMD) and bone microarchitectural deterioration. BMD is measured with dual x-ray absorptiometry (DXA). The aim of this study is to determine the importance of BMD and T-score in predicting bone fracture risk in patients sustained a minimal trauma fracture (MTF) of the hip. DXA estimation was conducted on 42 patients accompanied by 5-year follow-up period with result of 10 MTFs. The mean and SD value for hip BMD was 0.897 ± 0.132 g/cm^2 and T - score was -0.733 ± 1.179. In logistic regression we found more predictable value for BMD than T – score (β coefficient = -14.429, P = 0.0092). Sensitivity/specificity pair (91.4%/93.75%), BMD cutoff value = 0.793 and Youden index generated by BMD receiver operating characteristics (ROC) curve are more predictable in detection of hip MTF (P = 0.3464) than T - score sensitivity/specificity pair (82% and 53.13%). By ROC curve we found no statistical significance between pairwise comparison of both Area Under Curve (AUC) (0.838 and 0.769 for hip BMD and hip T - score, respectively). We concluded that hip BMD has greater predictable value in prediction of bone fracture risk than hip T - score in anteroposterior DXA estimation.

Keywords: *Bone Mineral Density; DXA; T-Score; ROC; AUC*

Introduction

Osteoporosis is the most common metabolic bone disease and can result in risk of bone fractures which increases with ageing. It is characterized by low bone mass and bone microarchitectural deterioration [1]. Bone mineral density (BMD) is considered to be a standard measure in diagnosing the osteoporosis and the assessment of risk fracture. These latest data, support the correlation of atherosclerosis and osteoporosis, indicating the parallel progression of two tissue (bone and vascular) destruction process with increased fatal and nonfatal cardiovascular events, as well as higher fracture risk [2].

BMD measured with dual x-ray absorptiometry (DXA), is expressed in absolute terms as grams of mineral per square centimeter scanned (g/cm2). Absolute BMD values are only meaningful in the context of what is normal for a measurement made at the same site in an individual with the same characteristics. The T - score is reported as the number of standard deviations (SD) where a patient's bone mineral density value is above or below the reference value for a healthy thirty-year-old adult. Osteoporosis was subsequently defined by the SD rather than by an absolute value of BMD. The World Health Organization (WHO) T - score cutoff value for osteoporosis is "–2.5", for osteopenia from "-1" to "-2.5" SD and normal BMD is within 1SD ("+1" to "-1") [3]. Fracture risk increases approximately twofold for every SD below the mean for a young adult [4]. The relationship is site-specific, where the measurement of BMD at the proximal femur

provides the optimal assessment of the risk of hip fracture. The greater negative number - more severe the osteoporosis. Although not everyone who has low bone mass will develop osteoporosis, everyone with low bone mass is at higher risk for the disease and the resulting fractures and minimal trauma fractures (MTF) [5]. The MTF are defined as fractures resulting from trauma ≤ a fall from standing height.

The aim of this prospective longitudinal study is to determine the importance of BMD and T-score for predicting the bone fracture risk in patients sustained a minimal trauma hip fracture.

Materials and Methods

During two month period, from 5th February to 7th April 2010, DXA estimation was successfully conducted on 42 consecutive patients (male 6, female 36) with mean age of 58.6 ± 9.9 years with their Body Mass Index (BMI) of 28.18 ± 4.23 kg/m^2. Fourteen patients were smokers, 15 were diabetics and 12 were hypertensive. Anteroposterior (AP) projection of DXA assessed femoral neck BMD. All of the patients were accompanied by 5-year follow-up period. DXA measurement of BMD is based on the difference in absorption of the high and low level X-ray beams across soft and mineral density tissue. The DXA scanner software has calculated the difference of the bone density measurement and of the soft tissue measurement.

BMD assessments

Because the neck of the femur BMD has been considered the gold standard, BMD around the hip is ideal when predicting the risk of fractures [6]. We assessed hip measuring using DXA scanner QDR4500SL by Hologic (Hologic Inc., Bedford, MA, USA) in femoral neck location. Before we started scanning, we prescanned desired anatomic area to find the best femur neck or lumbar spine position in region of interest (ROI). After the scan was finished, we selected the icon "Analyze Scan" to get specific data acquired by the previously made scan: area (cm^2), BMD and T - score [7]. DXA results are shown as the average values of repeated DXA measurement BMD (g/cm^2) once a year. All participants signed an informed consent and the Ethics Committee of our institution approved the study.

Statistical analysis

The data were analyzed using SPSS version 20.0 (IBM Co., Armonk, NY, USA). Student test for unpaired data was used to compare the subgroups with or without MTF. The BOX-and-Whisker diagram was plotted by MedCalc for Windows, version 15.8 (MedCalc Statistical Software bvba, Ostend, Belgium). Results are expressed as means ± SD or percentage. Receiver operating characteristics (ROC) curve analysis assessed distinction between patients with or without MTF and appropriate cutoff value for BMD and T – score. The incidence of fractures and number at risk were analyzed using Kaplan-Meier survival curves. The logistic regression model was used to identify the independent determinants of fractures predictors. Survival rates were analyzed using a plot of the Kaplan-Meier survival function.

Results

The mean and SD, range and median values for hip BMD, T - score, BMI, age and other demographic data are presented in table 1. The mean follow-up period was 31.7 ± 20.3 months (median 35 months) and 96 % confidence interval (CI) for the mean was 11.176 to 46.224 months.

Characteristic	Value (mean ± SD) or %	Range	Median
Age (years)	58.6 ± 9.9	37 - 79	61
Height (cm)	169.07 ± 10.6	152 - 193	168
Weight (kg)	80.7 ± 15.2	60 - 120	77.5
BMI (kg/m^2)	28.18 ± 4.23	21.63 - 38.74	27.58
BMD HIP (g/cm^2)	0.897 ± 0.132	0.665 - 1.298	0.862
T-score HIP	-0.733 ± 1.179	-4.6 to 2.3	-0.862
Sex No. (%)	Female 36 (85.71%)	/	/
Hypertension	12 (28.5%)	/	/
Smoking	14 (33.3%)	/	/
Diabetes	15 (35.71%)	/	/
HIP fracture, No. (%)	10 (23.81%)	0 to 1	0

Table 1: *Demographic characteristics of the patients studied.*

Sudden events caused by low-energy hip fractures, or MTFs were recorded in 10 patients (23.81%) during follow-up period and were marked by 1 (one). We used "0" (zero) or 1 (one) as binary variables to indicate the absence or presence of the sudden event hip fracture, respectively.

Comparison between subgroups

The comparison of mean BMD values in two subgroups according hip fractures (with or without hip fractures) by t test for unpaired data is presented in figure 1.

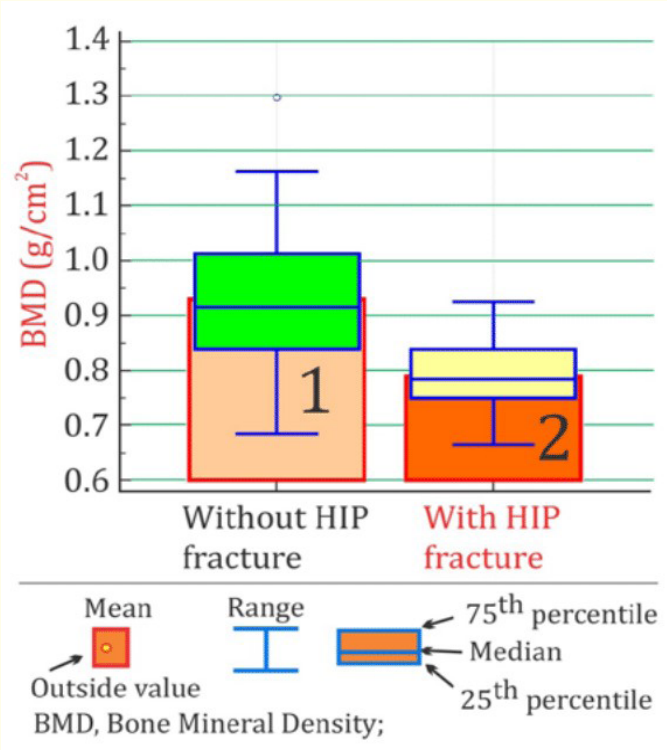

Figure 1: *Box-and-Whisker diagram of BMD in cases with or without hip fracture (t test for unpaired data).*

There was statistically high significance between the mean BMD in the subgroup 1 (without hip fracture) and subgroup 2 (with hip fracture). The mean value and SD of BMD in case with or without HIP fracture are: 0.789 ± 0.083 g/cm^2 vs. 0.930 ± 0.127 g/cm^2, test statistic t = -3.911, assuming equal variances (P = 0.0003) or assuming unequal variances (P = 0.0001). The F - test for equal variances (P = 0.096).

Kaplan – Meier curve

Survival rates (the period before hip fracture) were analyzed using Kaplan-Meier survival curves (Figure 2). Both red thin lines represent the CI, and the central red thickened line represents the survival curve function. A plot of Kaplan - Meier estimate of the periods before hip MTF, presented as series of horizontal steps of declining magnitude is shown in figure 2. Every vertical curve drop indicates an event (MTF).

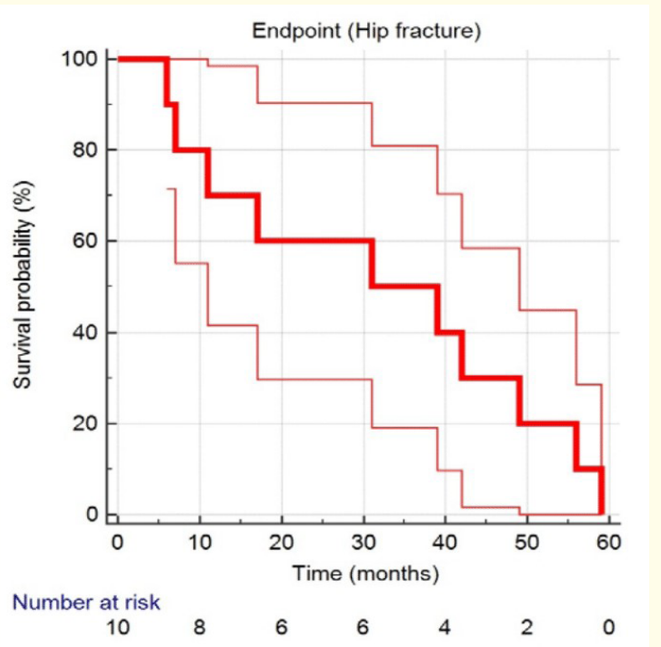

Figure 2: *Kaplan–Meier estimates of survival of patients during 5-year follow-up and number at risk for hip fracture.*

The mean and median survival (the period without hip fracture) was: 31.7 ± 6.42 months (31 months) and 95 % Confidence Interval for the mean was 19.116 to 44.284.

Logistic regression

We used logistic regression model because the dependent variable (hip fracture) is categorical. This binary dependent variable can take only two values ("0" and "1", without or with a fracture) which represent outcomes. The coefficients and standard errors (SE) parameters (β coefficient, st. error, Wald and p value are presented in table 2).

Logistic regression				
Dependent Y	Hip fracture			
Method	Backward			
Enter variable if P <	0.1			
Remove variable if P >	0.5			
Sample size				42
Positive cases				10 (23.81%)
Negative cases				32 (76.19%)
Chi-squared				11.943
DF				1
Significance level				P = 0.0005
Cox and Snell R^2				0.2475
Co-efficients and Standard Errors				
Variable	β coefficients	St. Error	Wald	P
BMD (g/cm^2)	-14.429	5.539	6.784	0.0092
Area under the ROC curve (AUC)				0.838

Table 2: *Logistic regression of categorical dependent variable (hip fracture) in dependency of BMD.*

There is statistically high significance (P = 0.0092) in logistic regression of hip BMD in prediction of hip fracture.

There is no statistical significance (P = 0.779, β coefficient = -0.679, Wald = 3.107, AUC = 0.769) in logistic regression of hip T-score in prediction of hip fracture. The absolute BMD value is more predictable variable in detection of hip fracture (P = 0.0092, β coefficient = -14.429, Wald = 6.784, AUC = 0.838).

Estimation of cutoff point

We used ROC curve analysis to distinguish the patients with or without hip fracture. Every single point on the ROC curve represents a sensitivity/specificity pair corresponding to a particular decision threshold (BMD or T - score in the detection of hip fracture). The Youden index table (we present only essential data) shows for BMD and T - score data for a sensitivity/specificity pair and Youden index for both ROC curves (dark blue line with orange squares for BMD and light blue line with dark blue point for T - score). For BMD: sensitivity 91.4%, specificity 93.75% (associated criterion BMD = 0.793, Youden index (J) = 0.6375) and for T - score: sensitivity 82%, specificity 53.13% (associated criterion T - score < 0.8, J = 0.5313). Sensitivity/specificity pair and J index generated by BMD ROC curve are more predictable in detection of hip MTF (P = 0.3464). The J index is the maximum vertical distance between the ROC curve and the diagonal line. It is an equivalent to maximize the sum of sensitivity and specificity for all the possible values of the cutoff point. The BMD J index is bigger than T - score J index (0.793 vs. 0.5313). The ROC curve comparison is presented in figure 3.

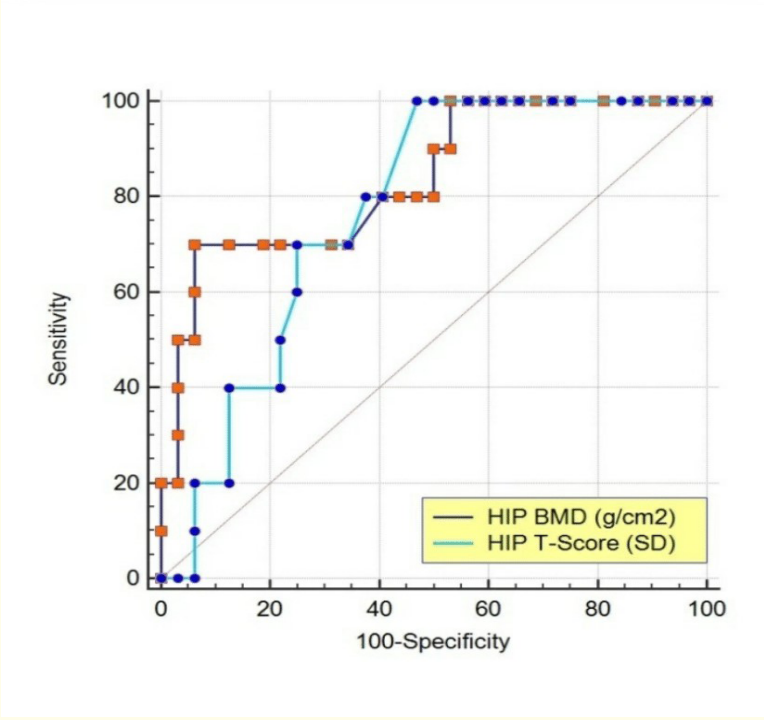

Figure 3: *Receiver operating characteristics (ROC) curves comparison for BMD and T-score as a predictors of hip fracture.*

The results of ROC curves comparison were: Area Under Curve (AUC) = 0.838 and 0.769 for hip BMD and HIP T - score, respectively. There was no statistical significance between pairwise comparison of both ROC curves (P = 0.3464, difference between areas = 0.0688, z statistic = 0.941). Pierson product-moment correlation (bivariate correlation) as a measure linear correlation between two variables x (hip BMD) and y (hip T - score) shows strong positive linear correlation (r = 0.696, p < 0.0001).

The figure 4 and figure 5 presented representative samples of original summary DXA reports for neck BMD and lumbar spine BMD and their T-score and Z-score, with demographic data: sex, ethnicity, age, height and weight. The DXA report presents the WHO classification (osteopenia or osteoporosis) and fracture risk for both regions.

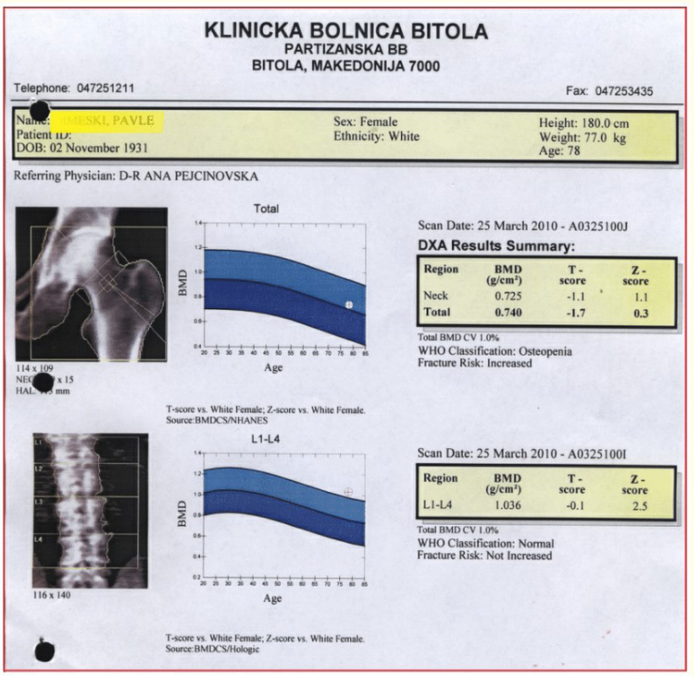

Figure 4: *Summary DXA results from 78 age female patient without future hip fracture.*

Figure 4 shows the hip BMD result classified as osteopenia with increased hip fracture risk of 78 age female patients who did not suffer hip fracture during the 5-year observed period. The lumbar spine BMD results, which do not relate to research in our study are classified as normal with not increased fracture risk.

I am apologize about the three dark black circles in the left side of the scanned DXA document which originate from the perforations intended for placing the sheet in the documents archive.

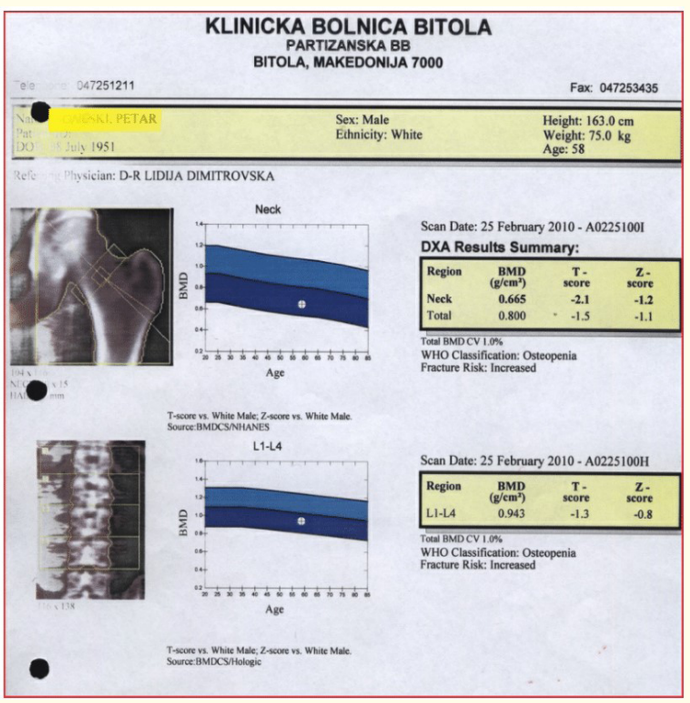

Figure 5: *Summary DXA results from 58 age male patient with future hip fracture.*

Figure 5 shows the hip BMD result classified as osteopenia with increased hip fracture risk of 58 age male patients who suffered hip fracture in first ten months during the 5-year observed period. The lumbar spine BMD results, which do not relate to research in our study are classified as osteopenia with increased fracture risk.

Discussion

In this prospective longitudinal study with 5 years of follow-up, we studied a cohort of 42 patients with a mean follow-up of 31.7 ± 20.3 months. Each participant was subjected to DXA diagnostic procedure to estimate BMD and T – score for predicting the bone fracture risk in patients sustained a hip MTF. Because low BMD is considered to be one of the major risk factors for hip fracture [8], we focused our attention to estimating BMD in femoral neck region. Another reason for choice of this region estimation is the fact that among all osteoporotic fractures, hip fractures are the location most commonly associated with mortality [9]. BMD have shown to be associated with mortality independently of age, weight, BMI, smoking status, previous fracture, physical activity, drug use, and presence of chronic disease [10]. We estimated and presented only the BMD DXA results (not lumbar spine BMD) because many studies have found that hip measurements may be superior to spine measurements for overall osteoporotic fracture prediction [11-13]. Usually, conventional AP DXA measurements provide greater value for spine BMD than the hip BMD. The main reason for the greater BMD in the spine than the femoral neck may lie in the fact that DXA relied on measurement of the relative absorption of dual energy X-ray beams blindly projected through the body. The dense aortic calcification rather than the spine absorbs the X-ray causing a falsely elevated BMD reading [13,14].

The patients with a higher score of aortic calcification results with more X-ray absorption expressed with an elevated spine BMD value [15]. Vertebral BMD is usually measured in the AP plane, though this method may falsely give high values in the presence of lumbar spondylosis or osteoarthritis, especially when associated with osteophytes and aortic calcification in the same time [13,15]. That is why, for all of the reasons listed above, we decided to present only the results of hip BMD instead both hip BMD and lumbar spine BMD.

The start point for making visible differences in BMD between patients with and without MTF is to compare them. The subgroup 1 (without hip fractures) has higher hip BMD than the subgroup 2 (with hip fractures) ($p = 0.0001$). This apparent BMD difference in both subgroups is not sufficient indicator that it can be a predictor of hip fractures. BMD is only one of many contributors to bone strength and fracture risk reduction. Bone strength is derived from bone quantity, which consists of density and size, and bone quality, which, in turn, consists of micro and macroarchitecture structure, material properties, and turnover [16]. Other important risk factors for hip fracture include a set of clinical risk factors identified by the WHO, including age, cigarette smoking, systemic glucocorticoid therapy > 3 months, MTF after age 50, parental hip fracture, alcohol use, rheumatoid arthritis and secondary osteoporosis [17].

We estimated by logistic regression that hip BMD has more predictable value in fracture risk prediction than hip T – score ($p = 0.0092$). Because it's no statistical significance ($p = 0.779$) a variable T – score is removed from model of regression. The J index and ROC curve analysis data shows that hip BMD because it's better sensitivity and specificity compared with hip T - score is more predictable in detection of hip MTF. The bigger J (0.793 vs. 0.5313), the bigger AUC (0.838 vs. 0.769) and bigger pair sensitivity/specificity for hip BMD than the hip T - score, give us the right to emphasize the meaning of hip BMD as a predictor of hip MTF. A femoral neck BMD T-score is a strong risk factor for predicting fracture risk and is a key factor in diagnosing osteoporosis in many studies and countries [18,19]. However, because of hip BMD and T - score strong positive linear correlation, is clear that relying on a T – score of < - 2.5 precludes diagnosing and treating many older persons at high risk for fracture based only by hip BMD estimation. A lot of studies appreciate that the number of fractures is higher in the osteopenic group than in those with osteoporosis based on T scores [20]. Women with vertebral fractures are considered to have clinical osteoporosis even if they have hip T - scores in the osteopenic range, but not low hip BMD [21]. Our and other studies emphasize the significance of BMD rather than T - score in fracture risk prediction, especially based on BMD cutoff (0.793 g/cm^2). In our relatively smart cohort this BMD cutoff point with sensitivity/specificity pair greater than 90% has more predictable value than the same of T – score [20,21]. We do not use the novel Fracture Risk Assessment tool (FRAX), more predictable software than BMD or T – score only, software for identifying younger women at higher risk of fracture. The FRAX tool can be used as an assessment modality for the prediction of fractures on the basis of clinical risk factors, with or without the use of femoral BMD. The FRAX® algorithms give the 10-year probability of hip fracture and 10-year probability of a major osteoporotic fracture (spine, forearm or shoulder fracture).

Conclusion

Knowing the BMD cutoff value (0.793 g/cm2) we can predict the risk for MTF for all patients who have value above that, not only for hip but also for fractures in other localizations. The T-score should be an additional parameter for the improvement of the risk assessment, smothering the BMD as the basic risk indicator. We conclude that hip BMD has more predictable value in prediction of bone fracture risk than hip T - score.

Conflict of Interest

No one from the all authors have received research grants from the any companies. All of the authors declare that they have no conflict of interest.

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Volume 7 Issue 4 August 2017