Journal of Dentistry & Oral Disorders

Open Access

Austin Publishing Group

Research Article

High Bone Mineral Density: Real or Masking a Bone Fragility?

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Received: September 05, 2017; **Accepted:** October 13, 2017; **Published:** October 20, 2017

Abstract

Objective: The aim of this study is to evaluate individuals with high BMD and correlate with clinical and laboratory parameters.

Methods: We performed a search over the last 4 years, in the boned ensitometry database of the endocrinology unit (Hospital de Clinic as, Federal University of Parana), searching for Z-score ≥ 2.0 SD in spine or femur. After selection, we reviewed the medical records of each patient, evaluating their co morbidities and medical history, In a subgroup of patients, we performed an analysis of trabecular bone score.

Results: 104 patients were included, the mean age was 62 years, majorities (96%) were women. A significant correlation between the presence of artifacts and altered BMD (p <0.001) was observed. In patients with high bone density in spine, approximately 58% had osteopenia or osteoporosis at one or more sites evaluated, whereas in patients with arthrosis in spine, 68% had a diagnosis of osteoporosis or osteopenia. Furthermore, a correlation between artifacts and Z-score ≥ 2.0 SD in the femoral neck was found (p = 0.008). Of all co morbidities analyzed, there was an association between hypertension and presence of artifacts (p <0.001), such as arthrosis and scoliosis. It was also observed that 72% of patients with hypothyroidism had artifacts (p=0.014).The analysis of trabecular bone score was performed in a subgroup of 21 postmenopausal women, and damage to the micro architecture was observed in 39% of patients with normal densitometry.

Discussion & Conclusion: We found a high prevalence of patients with high bone mass in one site and diagnosis of osteopenia / osteoporosis with micro architecture damage. These results show that patients with artifacts in the densitometry exam need a more careful evaluation.

Keywords: Artifacts; High bone mineral density; Osteopenia; Osteoporosis

Introduction

The World Health Organization defines the presence of osteoporosis in postmenopausal women as a Bone Mineral Density (BMD) less than or equal to 2.5 standard deviation (SD) (T score -2.5) compared to young women, assessed by densitometry of lumbar spine, femur, or forearm [1]. In this context, bone density is considered normal when it is greater than or equal to -1.0 standard deviation (T-score -1.0) [2]. However, there is no cut-off point above which bone density can be determined as abnormally high, meaning that T-score values equal to or greater than 4 to 5 SD, for example, are not clinically appreciated. It is known that degenerative diseases, vascular calcifications, and compression fractures can lead to localized increase in BMD. On the other hand, when the increase in BMD is widespread, it may be associated with genetic disorders, and a variety of endocrine, metabolic, infectious, or neoplastic diseases [3].

In a consensus published in 2007, the International Society for Clinical Densitometry concluded that it is not possible to establish a cut-off point for high BMD since there is insufficient evidence to determine whether a person with high BMD has some underlying disease or higher risk of fracture [2]. Whyte [3] suggested that the Z-score, not the T-score, is better to evaluate high BMD, with a threshold ≥ 2.5 SD. The Canadian consensus also suggests that a Z-score above 2.5 should not be considered normal [4]. Thus, if a Z-score ≥ 2.5 DP is used to define high BMD, the estimated prevalence is 6.2/1000, while a Z-score ≥ 4 SD identifies approximately 3/1000, significantly decreasing the prevalence of this finding [5].

Multiple causes of high BMD that have been identified include artifacts, fractures, ligament calcification, degenerative changes [2], diffuse idiopathic hyperostosis [6], aortic calcification, and osteoarthritis [7]. However, until now, no consensus has been reached on the definition of high bone density and its clinical significance.

Despite the BMD measurement being recommended to evaluate the risk of fracture, it does not directly reflect the deterioration in bone micro architecture. The Trabecular Bone Score (TBS) is a noninvasive technique that can be applied to X-ray images by quantifying local variations in gray level. It is comparable to BMD to predict fractures, and the combination was superior to either measurement alone [8]. Furthermore, TBS is an indirect measurement of trabecular micro architecture that is not affected by lumbar osteoarthritis [9,10].

The aim of this study is to evaluate the clinical profile of

Citation: Fighera TM, Silva RP, Pinto JVM, Cardenaz GS, Moreira CA and Borba VZC. High Bone Mineral Density: Real or Masking a Bone Fragility?. J Dent & Oral Disord. 2017; 3(5): 1074.

Table 1: Final densitometric diagnosis and anthropometric variables.

	Normal	Osteopenia	Osteoporosis	p
Age (years)	55 ± 10,438	67 ± 11,788	75 ± 12,755	<0.001
Weight (kg)	78 ± 13,669	65 ± 13,233	59 ± 10,942	<0.001
BMI (kg/m²)	31 ± 5,63	27 ± 5,21	26 ± 4,85	<0.008

BMI: Body Mass Index

Table 2: Association between comorbidities, artifact and FDD.

	Number of patients (%)	Artifact (*p*)	FDD (*p*)
Hypertension	62	0.00*	0.393
COPD	4	0.392	0.789
Arthrosis of upper limbs	4	0.562	0.537
Arthrosis of lower limbs	15	0.129	0.69
Diabetes	22	0.32	0.975
Dyslipidemia	39	0.969	0.438
Depression	21	0.505	0.906
Varicosis veins	7	0.057	0.481
Hypothyroidism	18	0.014*	0.06
Obesity	13	0.28	0.065
Chronic renal failure	1	0.51	0.453
Asthma	3	0.162	0.252

FDD: Final Densitometric Diagnosis; COPD: Chronic Obstructive Pulmonary Disease; Artifacts: Arthrosisandscoliosis. *p<0, 05

individuals with high BMD and correlate it with laboratory tests, TBS and presence of artifacts in bone densitometry.

Materials and Methods

We evaluated all Bone Mineral Density (BMD) exams performed between January 2009 to December 2012 in the endocrinology unit, Hospitalde Clinicas (UFPR), searching for results with Z-score ≥ 2.0 SD in lumbar spine and/or femur. Inclusion criteria were men and women between 20 and 88 years; with medical records available at the hospital file; and not currently participating in clinical research. From medical records were collected anthropometric data, history of physical activity, smoking and past fractures, presence of co morbidities (analyzed only when present in two or more patients), and possible co morbidities that could be associated with a high BMD in medical history. Laboratory tests such as measurement of serum calcium, phosphorus, albumin, creatinine, 25 hydroxy-vitamins D (25OHD), and Parathormone (PTH) were also evaluated. The same technician performed the BMD tests by Dual Energy X-Ray Absorptiometry (DXA) on a Lunar Prodigy whole-body scanner (GE Medical Systems, Madison, WI, USA).TBS was performed in a subgroup of postmenopausal women with available lumbar spine densitometry.

Images of densitometry were reanalyzed and patients classified according to the presence of possible artifacts in the lumbar spine, such as presence of degenerative disease (osteoarthritis), scoliosis, or both, or any visible artifact that could be characterized as a factor for increasing bone mass. Subsequently, we classified patients based on the Final Densitometric Diagnosis (FDD) as normal, osteopenia, and osteoporosis, according to WHO and ISCD criteria (International Society for Clinical Densitometry), and above normal when the Z score was ≥ +2.0SD in at least two sites analyzed.

Statistical analysis

Data were entered in Excel and then exported to SPSS v.18.0 for statistical analysis. Categorical variables were reported as frequencies and percentages. Quantitative variables with normal distributions were described by mean and standard deviation, and the asymmetric distribution with the median and inter quartile range (25^{th} and 75^{th} percentiles). Categorical variables were associated with the Chi-square test or Fisher's exact test. Quantitative variables with normal distributions were compared by Analysis of Variance (ANOVA) followed by Tukey's post hoctest to locate differences. Quantitative variables with asymmetric distribution were compared between two categories using the Mann-Whitney test and between three categories using the Kruskal-Wallis test. To assess the correlation between quantitative variables, the Pearson correlation coefficient was used, with the significance level set at 5%.

Results

The final sample included 104 patients with mean age of 62.4±14.3 years, 96% were women. The mean weight was 70.3±14.5 kg, and the body mass index (BMI) was 29±5.5 kg/m². Most patients were Caucasian (99%), and 11% were smokers. Of the total sample, only 9 patients (9%) practiced regular physical activity, considered at least30minutes of daily exercise. Half of the patients used some treatment for osteoporosis, especially bisphosphonates, approximately 20% had used or were using glucocorticoids, and 13% were taking hormone replacement therapy.

Degenerative disease [arthrosis] (40%), scoliosis (3%), or both (12%) were the artifacts present in this sample. The mean BMD in the lumbar spine was 1.447 ± 0.219 g/cm²; in the femoral neck, 1.019 ± 0.272 g/cm²; and in the forearm, 0.766 ± 0.129 g/cm². When evaluated the FDD, 60 individuals (57.6%) had low bone mass reported in another site, being 41 (39.4%) and 19 (18.2%) with osteopenia and osteoporosis, respectively. When patients with artifacts in the lumbar spine were excluded, only 24.2% had osteopenia and 6.1% had osteoporosis at the FDD. Low bone mass was present in 68.5% of the 42 patients with vertebral arthrosis (51.4% had osteopenia and 17.1% had osteoporosis at the FDD), with a significant association between the presence of artifact and low bone mass in the FDD (p<0.001). No association was found between the presence of artifacts in lumbar spine and the Z-score > 2.0 SD in this site (p = 0.537) or in the total hip (p = 0.299). However, a significant association was found between the presence of artifacts and Z-score > 2.0 SD in the femoral neck (p = 0.008). Only 25% of the patients without a diagnosis of arthrosis showed high BMD.

Significant differences were found among age, weight, and BMI according to the FDD (Table1). No significant association was found between the FDD and other clinical parameters evaluated. Patients with high bone mass had a higher number of co morbidities (p= 0.018). Of all co morbidities observed, there was an association between hypertension and hypothyroidism and the presence of artifacts (Table 2). About 72% of patients with hypothyroidism had artifacts, but not higher BMD. No association was found between the final diagnosis and medications for osteoporosis or abnormal laboratory test (p =0.381 and p= respectively).

The values of BMD in the femoral neck and spine were significantly associated (p <0.001). In the sub group of patients with high BMD at the spine and femur (n =27), [11] (78%) had the FDD of high bone mass. Compared to patients with a FDD of osteoporosis or osteopenia, those with high BMD at both sites were younger (57±16 *vs* 70±12years) (p =0.009) and had higher weight (72±13 *vs* 64±12 kg) (p =0.001). There was no difference regarding smoking history (p =0.635), family or personal history of fracture (p =0.090), and use of medications for osteoporosis treatment (p =0.107).

TBS was performed in [11] postmenopausal women, with a mean of 1.373 (1.093 – 1.530). Among them, [12] were normal, [7] had partial damage of the micro architecture, and [1] had degraded micro architecture. Considering the patients with normal densitometry, 39% had damage in the micro architecture by TBS. No correlation was observed between TBS and BMD (p = 0.164).

Discussion & Conclusion

Bone densitometry presenting a Z-score above 2.0 SD, performed in our center over a period of about [4] years, were selected and analyzed. The mean age was 62 years, and over 90% of the study sample was women, with mean BMI of 29 kg/m^2. The sample was consistent with other studies, with a significant prevalence of women over 50 years and increased bone mass associated with higher BMI. The causes of high BMD in the setting of increased body weight are not completely understood, but include the estrogen production in the fat tissue and the extra weight carried by the skeleton [13]. The analysis of patients with increased BMD in the spine revealed that approximately 58% had osteopenia or osteoporosis at one or more sites, whereas in patients with arthrosis, 68% had a diagnosis of osteoporosis or osteopenia. In a study of [12] hospitals in the UK, 5/1000exams showed a Z score≥+4, and approximately half of the cases were associated with artifacts caused by degenerative osteoarthritis. Clinical suspicion of osteoporosis in 35% and presence of co morbidity in 22% was the reason for the high BMD patients to perform a BMD test [14]. The presence of art if acts in densitometry is an important cause of false increase in BMD, and should be considered in the presence of a suggestive clinical history, since it can mask the diagnosis of osteoporosis. Osteoarthritis can raise the calcium content in densitometry due to abnormalities in the margins of the vertebrae caused by sclerosis and osteophytes, which mainly occurs in the lumbar spine and justifies the finding of upward progression of BMD at this site [12], even the presence of few osteophytes may increase BMD by 24% [15]. On the other hand, the effect of osteoarthritis on BMD of the femuris minimal [16], however we found a significant correlation between the presence of artifact and Z-score>2.0 SD in the femoral neck. This finding may be explained by the older age and high weight. Furthermore, no association was found between the co morbidities analyzed and FDD. In our sample, patients with osteoporosis had lower weight and BMI, as well as older age, when compared with patients with osteopenia and patients with normal densitometry, which is consistent with the literature [11]. There was a direct and significant association between the values of BMD at the femoral neck and spine regardless the high prevalence of artifacts.

Other artifacts associated with high BMD are diffuse idiopathic hyperostosis [17], vertebral fractures [18], ankylosing spondylitis [19], calcification of intra-abdominal structures such as the aorta [12], deposits of iron in patients with thalassemia major [20], kidney stones [21], and silicone implants into the gluteal area [11]. Significant changes in BMD measurement can be caused by some focal abnormalities, such as Paget's disease [12] and some tumors [22]. Finally, osteopetrosis, the characteristic disease of high bone density [23], was detected only in one patient of our sample. We found no reference in the medical records regarding other diseases associated with high BMD.

Our results showed an association between the diagnosis of hypertension and the presence of artifacts in densitometry. Although there are no data in the literature demonstrating this association, there are studies linking increased bone mass and use of antihypertensive drugs [24]. The same relation was observed in patients with hypothyroidism. There are some controversies regarding the direct effect of TSH maintaining bone mass, and its indirect effect by reducing bone metabolism. Although the thyroid hormones have catabolic effects on bone tissue, hypothyroid is misassociated with increased risk of fractures, even in patients with subclinical disease [25]. Therefore, the association between hypothyroidism and artifacts that interfere with the BMD can have a significant impact in the assessment of fracture risk of these patients.

In the TBS subgroup, approximately 40% of the patients with a normal densitometry presented damage in micro architecture. This high prevalence may be justified because TBS is not affected by degenerative diseases such as osteoarthritis. Kolta and cols [25] evaluated 1.254 postmenopausal women with a mean age of 66.7±7.1 years. The presence of osteoarthritis significantly increased BMD, but there was no difference between TBS values.

We found that a Z-score > 2 does not necessarily indicate a normal BMD. Artifacts and metabolic disorders seem to be associated with this finding. Some patients may have their bone mass over estimated in one or more sites in densitometry, and it is important to recognize these individuals and the possible associated factors that may mask a situation of bone fragility. This study shows the importance of densitometric analysis of at least two sites, especially in those patients who have degenerative disease, and further evaluation with TBS may be useful. Larger and prospective studies are needed to clarify the impact of these changes in the risk of bone fractures.

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J Dent & Oral Disord - Volume 3 Issue 5 - 2017
ISSN: 2572-7710 | www.austinpublishinggroup.com

Citation: Fighera TM, Silva RP, Pinto JVM, Cardenaz GS, Moreira CA and Borba VZC. High Bone Mineral Density: Real or Masking a Bone Fragility?. J Dent & Oral Disord. 2017; 3(5): 1074.