Original Article

Less influence of body mass index on bone mineral density of radius as compared to proximal femur: Possible role in the diagnosis of osteoporosis

ABSTRACT

It has been shown that body mass index (BMI) and obesity may affect the mineral density of bones, regionally on weight-bearing bones or systemically through hormones and cytokines. The objective of this study was to evaluate the effect of BMI on bone mineral density (BMD) of the radius. In this cross-sectional study, 260 patients, 233 postmenopausal women and 27 men over 50, were included who underwent a bone densitometry scanning using dual-energy X-ray absorptiometry after obtaining an informed consent. The scanning was performed in three areas (i.e., spine, proximal femur, and radius), then densitometric data (BMD, T- and Z-score) were extracted. Regression analysis was performed to evaluate the effect of independent variables of age, gender, and BMI on the BMD of the above regions. By grouping the patients in two categories (BMI <25 as normal or underweight and BMI >25 as overweight and obese), the discordance in the diagnosis following the inclusion of radius into interpretation (diagnosis based on 2 vs. 3 areas), was assessed by an agreement test. The study is approved by the ethics committee of the university. Of 260 participants in the present study, mean and standard deviation for age were 61.48 ± 8.95 for all patients, 65.81 ± 10.59 for male and 60.98 ± 8.62 for women. An increasing effect of BMI was found to be statistically significant in weight-bearing areas (total femur and femoral neck) and BMI increase was not associated with increased BMD of radius. An agreement test between two diagnoses is used that showed a discordance of 28.5% in diagnosis (diagnosis based on 2 vs. 3 areas) with a kappa coefficient of 0.547 (P = 0.001). In total, 25.4% was minor discordance and 3.1% was major discordance. Based on the results of this study, it is concluded that the BMI is not associated with increased BMD in bones that are not weight bearing, such as radius. Therefore, it may be preferred to include the densitometric data of radius into the diagnosis.

Keywords: Body mass index, bone mineral density, obesity, osteoporosis, radius

INTRODUCTION

Obesity and osteoporosis are two major problems with high impact on health-care systems. Osteoporosis, as a common metabolic disease of the bone, comprises decrease in bone density or mass per volume as a result of resorption of the matrix of bony tissue.[1-4] The global incidence of osteoporosis-related fracture is 5 million each year, of which fracture of hip and vertebrae are more common. The distal radius is the most common site of occurrence of fracture in upper extremities and accounts more than one-sixth of fractures treated in the United States. The annual cost of these fractures has been estimated substantially high.[5-7] The risk of death from osteoporosis during a woman's life is estimated large, and thus, the impact of timely management of the risk factors, whether controllable or uncontrollable, is high in the outcome.[8,9]

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Obesity, in simple terms, is as an increase in body fat content and measured by body mass index (BMI) and is a known risk factor for cardiovascular and metabolic disorders. In contrast, it has been shown that it may have a protective effect on bone mineral density (BMD).[10-14] The exact mechanism is not clearly understood, but it is postulated that increasing body weight borne by bones stimulates bone synthesis.[15] However, other studies have proposed another mechanism, by which increasing production of inflammatory cytokines and specifically, tumor necrosis factor, and also secretion of sex hormones, for example, estrogen, by adipose tissues play a major role.[16,17] In addition, insulin resistance and elevated circulatory insulin level urge the ovary to produce androgens and estrogen. This, in turn, inhibits osteoclasts and activates osteoblasts.[18] Studies have shown other pathways of adipose tissue-derived molecules such as leptin and adiponectin, which have a negative and positive effect on the bone mass, respectively. Leptin also plays through a complex mechanism by influencing stem cells.[19,20]

The interrelationship between body weight/BMI and BMD of bones has been evaluated in a few studies, although conflicting results have been obtained. In studies by Alonso *et al*.[21] and El Hage *et al*.,[22] a positive correlation was found between weight and density of the radius. In another study, an association was found between muscle and fat masses and BMD.[23] The variation of weight, as weight loss or gain, on the mineral density of radius bone leads to a change of 0.7% and 0.4%, respectively.[24] As the bony structure and weight bearing status of the radius is different from hip and spine, in another study, about 20% of patients experienced a change in diagnosis, reclassification to higher levels following the inclusion of the forearm into densitometry reporting.[25] Although there is some inconsistency between the results of the previous studies regarding the effect of obesity and weight bearing on the BMD of the bones of spine, hip, and particularly radius, as reference regions for the diagnosis of osteoporosis, and whether the effect is systemic by hormonal mechanisms or is governed locally by exertion of pressure on bone, the present study is conducted. Moreover, the inclusion of radius into densitometry scanning and the possible impact on the final diagnosis, especially in obese patients, is also investigated.

METHODS

In this cross-sectional study, from the year 2016 to 2018, from more than 2000 patients referred to our department for bone densitometry scan, 260 patients, 233 postmenopausal women and 27 men over 50, were included consecutively after receiving an informed consent. The study was approved by the institutional ethics committee (letter number IR.SBMU.MSP.REC.1397.569 dated 20th November 2018). Patients with any history of radial fracture, rheumatologic disease, presence of known risk factors of osteoporosis, secondary causes of obesity such as endocrine causes, endocrine diseases, obesity (weights over 120 kg), defects in the spinal cords, pelvis and lower limbs, infertility, pregnancy and breastfeeding, acute or chronic renal failure, cancer and history of chemotherapy, chronic diarrhea or malnutrition, receiving Vitamin D supplementation, medications affecting BMD or treatment for osteoporosis, mental disorders, and smoking and alcohol consumption were excluded from the study.

Based on the WHO criteria, BMI below 18.5, between 18.5 and 25, and above 25 are considered as underweight, normal, and overweight, respectively.[8] Densitometry scans were conducted by the method of dual-energy X-ray absorptiometry by HOLOGIC® scanner (QDR series Explorer), according to the WHO standard procedural protocol in three areas of the proximal femur, spine, and radius of nondominant limb. Images were analyzed using the standard software provided by the manufacturer and data were extracted as BMD in g/cm^2, T- and Z-score by drawing regions of interest in the areas of the neck and total femur regions, L1 to L4 vertebrae, and 1/3 distal of radius. Using independent-sample *t*-test, the data of BMD, T- and Z-score in spine, total femur, femoral neck, and distal radius are compared in two groups (patients with BMI less than 25 vs. higher than 25). Based on the WHO criteria for diagnosis, T-score of −2.5 or less, between −2.5 to −1, and −1 and above is considered as osteoporosis, osteopenia, and normal, respectively.[26] The final diagnosis was made based on the two and three regions separately, and then the discordance was evaluated and classified as minor and major discordances.[27] Minor discordance means one level change in the diagnosis from normal to osteopenia or from osteopenia to osteoporosis and vice versa. Likewise, major discordance means a two-level change in the diagnosis, i.e., from normal to osteoporosis and vice versa.[25] After collecting data, multivariate regression was used to analyze the effect of gender, age, and BMI on the BMD results of the spine, hip, and radius areas using the SPSS software SPSS software IBM® SPSS® Statistics for Windows, Version 24.0, Chicago, IL, United States. The $P < 0.05$ was considered statistically significant. The study is approved by the ethics committee of the university.

RESULTS

Of 260 participants in the present study, 233 (89.6%) were female and 27 (10.4%) were male and age from 46 to 90 years. Mean and standard deviation for age were 61.48 ± 8.95 for all

patients, 65.81 ± 10.59 for male and 60.98 ± 8.62 for women. Mean and SD of BMI of the patients were 27.15 ± 4.15. Of 260 patients, 4 (1.5%), 79 (30.4%), 115 (44.2%), 51 (19.6%), 11 (4.2%) were regarded as underweight, normal, overweight, obese, severe obese, and morbid obese, respectively. Basic data including age, gender ratio (male-to-female), BMD, T- and Z-scores of patients in two groups of BMI <25 and higher than 25 is presented in Table 1. Comparing BMD, T- and Z-score of spine and radius between the two groups showed no statistically significant difference. However, at the regions of the total femur and femoral neck, the difference of BMD, T- and Z-score between two groups was statistically significant [Table 2]. Results of multivariate regression analysis are provided in Table 3. As can be seen, the variables of gender and age are effective in all regions, but BMI is effective in total femur and femoral neck regions. Per one unit of increase in BMI, BMD total femur increases by 0.258 on average, and femoral neck BMD increases by 0.007 on average, which are statistically significant. Pearson correlation between BMI and BMD of spine, BMI and BMD of femoral neck, BMI and BMD of total femur, and BMI and BMD of distal radius was 0.096 (P = 0.122), 0.255 (P = 0.000), 0.232 (P = 0.000), and −0.037 (P = 0.550), respectively. Scatterplots of BMD of the spine, femoral neck, total femur, and radius versus BMI are shown in Figure 1. In Table 4, the numbers and percentages of patients with concordance and discordance of diagnoses based on 2 and 3 areas, as a result of the inclusion of the data of the forearm, are presented. An agreement test between two diagnoses is used that showed a discordance of 28.5% with a kappa coefficient of 0.547 (P = 0.001). Of 28.5% discordance, 9.2% was from normal to osteopenia (minor discordance), 3.1% from normal to osteoporosis (major discordance), and 16.2% from osteopenia to osteoporosis (minor discordance). In patient with BMI more than 25, 32.3% discordance was found (28.3% minor and 4.0% major) and in patients with BMI below 25, 20.5% discordance were obtained (19.3% minor and 1.2% major).

Table 1: Basic data of patients as categorized by body mass index

Description	BMI <25 (*n*=83; 31.9%)	BMI >25 (*n*=177; 68.1%)
Age	61.36±8.66	61.54±9.10
Gender ratio (male-to-female)	0.12	0.11
Spine		
BMD	0.871±0.170	0.895±0.140
T-score	−1.62±1.50	−1.39±1.27
Z-score	−0.22±1.55	0.04±1.30
Total femur		
BMD	0.796±0.121	0.835±0.114
T-score	−1.25±0.97	−0.92±0.90
Z-score	−0.25±1.10	0.07±0.87
Femoral neck		
BMD	0.684±0.103	0.727±0.099
T-score	−1.52±0.94	−1.14±0.87
Z-score	−0.24±1.00	0.17±0.85
Distal radius		
BMD	0.587±0.083	0.581±0.088
T-score	−2.02±1.24	−2.02±1.35
Z-score	−0.60±1.21	−0.64±1.11

BMI: Body mass index; BMD: Bone mineral density

Table 2: Results of comparison of bone mineral density, *T*-and *Z*-score of spine, femoral neck, total femur, and radius

Description	Mean±SD difference	*P*
BMD		
Spine	−0.024±0.020	0.220
Femoral neck	−0.042±0.013	0.002*
Total femur	−0.039±0.015	0.012*
Radius	0.006±0.011	0.582
T-score		
Spine	−0.226±0.179	0.208
Femoral neck	−0.378±0.118	0.002*
Total femur	−0.325±0.122	0.009*
Radius	0.001±0.175	0.995
Z-score		
Spine	−0.257±0.185	0.166
Femoral neck	−0.410±0.120	0.001*
Total femur	−0.317±0.138	0.023*
Radius	0.029±0.152	0.848

**P*-values less than significance level or 0.05. SD: Standard deviation; BMD: Bone mineral density

DISCUSSION

In the present study, regression analysis revealed that per 1 year increase in age, BMD decreases by −0.477 in the lumbar area, −0.238 in the total femoral area, −0.002 in the femoral neck area, and −0.417 g/cm^2 in the radius area, which all of them were statistically significant, confirming some of the previous studies, including the study conducted by Alonso *et al.* in Brazil[21] and El Hage *et al.* in Lebanon.[22] Moreover, the results of this study showed that per one unit of increase in BMI, BMD in the lumbar area increased by 0.01 g/cm^2 on average, BMI values >30 did not result in a drop in BMI in the lumbar area and the values increased linearly. In addition, per one unit of increase in BMI, BMD in the total femoral area and femoral neck increased by 0.258 and 0.007 (g/cm^2), respectively, which was significant. In a study conducted by Lloyd *et al.*, results showed that per one unit of increase in BMI an amount of 0.0082 g/cm^2 in femoral neck BMD and 10 units of increase in BMI resulted in a change from the osteoporotic BMD level to normal BMD level,[28] which is similar to the result of the present study in the femoral neck region. In the radius area, per one unit of increase in BMI, BMD increased by 0.15 (g/cm^2), which was not significant. In general, these findings confirmed the

study conducted by Tóth *et al.*,[29] which showed a stronger association between BMI and femoral neck BMD and the study conducted by Silva *et al.* showed that BMI is the most important determinant of BMD in the femoral neck area.[30] However, the results were inconsistent with the results of the study conducted by El Hage *et al.* who reported obesity is associated with higher levels of BMD.[22] In the present study, BMI was not associated with higher BMD of the radius. Based on the regression analysis, it was shown that BMD values in women in the lumbar, total femoral, and radius areas were significantly lower than those in men. But in femoral neck area, the BMD value in women was higher than that in men (by 0.801 g/cm2), which was statistically significant. It can be due to higher BMI in the women population studied (27.2 ± 4.2 in women vs. 26.3 ± 3.6 in males). It can explain the augmenting role of weight bearing on BMD in femoral neck area. Finally, in the present study, to evaluate the final result, which is basically a judgment criterion based on the lowest value obtained, once the final result was evaluated based on two areas (hip and lumbar), then, the final result was re-evaluated by adding the third area (1/3 radius distal). Accordingly, there was 28.5% discordance between the final result based on two areas and the final result based on three areas, which is a very significant proportion of patients. Of these discordances, 9.2% of changes from normal diagnosis to osteopenia were minor discordance, 3.1% of changes from normal diagnosis to osteoporosis were major discordance, and 16.2% related to change from osteopenia to osteoporosis were minor discordance. In total, 25.4% was minor discordance and 3.1% was minor discordance. In the study conducted by Amiri *et al.*, 20% minor discordance and 0.8% major discordance were obtained,[25] which are lower than the values obtained in this study. Patient misdiagnosis is important in terms of management and treatment because if the patient is placed in the osteoporotic group following the misdiagnosis, there will be an urgent need to receive anti-osteoporosis treatment and if the patient is misdiagnosed from normal to osteopenia, he/she should receive preventive medical therapy and follow-ups with shorter intervals. In the present study, when the same study was performed in two subgroups of BMI >25 and BMI <25, the findings indicated 32.3% discordance in BMI >25 group and 20.4% discordance in the BMI <25 group, which suggests the need to add the third area (radius) in all patients undergoing bone mineral densitometry. Due to the higher discordance in the BMI >25 group, it is recommended to add a third area (radius) in patients with high BMI.

Table 3: The effect of independent variables of gender, age and body mass index on bone mineral density of the spine, femoral neck, total femur, and radius in regression analysis

Description	β coefficient	SD	*P*
Spine			
Gender	−0.515	0.017	0.000
Age	−0.477	0.001	0.000
BMI	0.010	0.002	0.864
Femoral neck			
Gender	0.801	0.069	0.000
Age	−0.002	0.020	0.000
BMI	0.007	0.001	0.000
Total femur			
Gender	−0.239	0.023	0.000
Age	−0.238	0.001	0.000
BMI	0.258	0.002	0.000
Radius			
Gender	−0.522	0.014	0.000
Age	−0.417	0.000	0.000
BMI	0.015	0.001	0.758

SD: Standard deviation; BMI: Body mass index

CONCLUSION

Finally, based on the results of this study, it is concluded that the augmenting role of overweight and obesity in the weight-bearing areas is more evident. Therefore, it is necessary to add the third area (1/3 of distal radius) to assess the bone densitometry in patients with high BMI and may pose a significant impact on the management of the patients.

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Table 4: Frequency and percentage of patients having diagnosis based on 2 and 3 areas in two groups of body mass index <25 and body mass index >25

Diagnosis based on 2 areas	Diagnosis based on 3 areas	BMI <25 (*n*=83; 31.9%)	BMI >25 (*n*=177; 68.1%)	All patients (*n*=260; 100%)
Normal	Normal	8 (9.6)†	16 (9.0)	24 (9.2)
	Osteopenia*	3 (3.6)	21 (11.9)	24 (9.2)
	Osteoporosis*	1 (1.2)	7 (4.0)	8 (3.1)
Osteopenia	Osteopenia	27 (32.5)	62 (35.0)	89 (34.2)
	Osteoporosis*	13 (15.7)	29 (16.4)	42 (16.2)
Osteoporosis	Osteoporosis	31 (37.4)	42 (23.7)	73 (28.1)

*Discordance between diagnoses based on 2 and 3 areas following inclusion of data of forearm into interpretation, †Numbers in parentheses denotes percentages of patients in each group. BMI: Body mass index

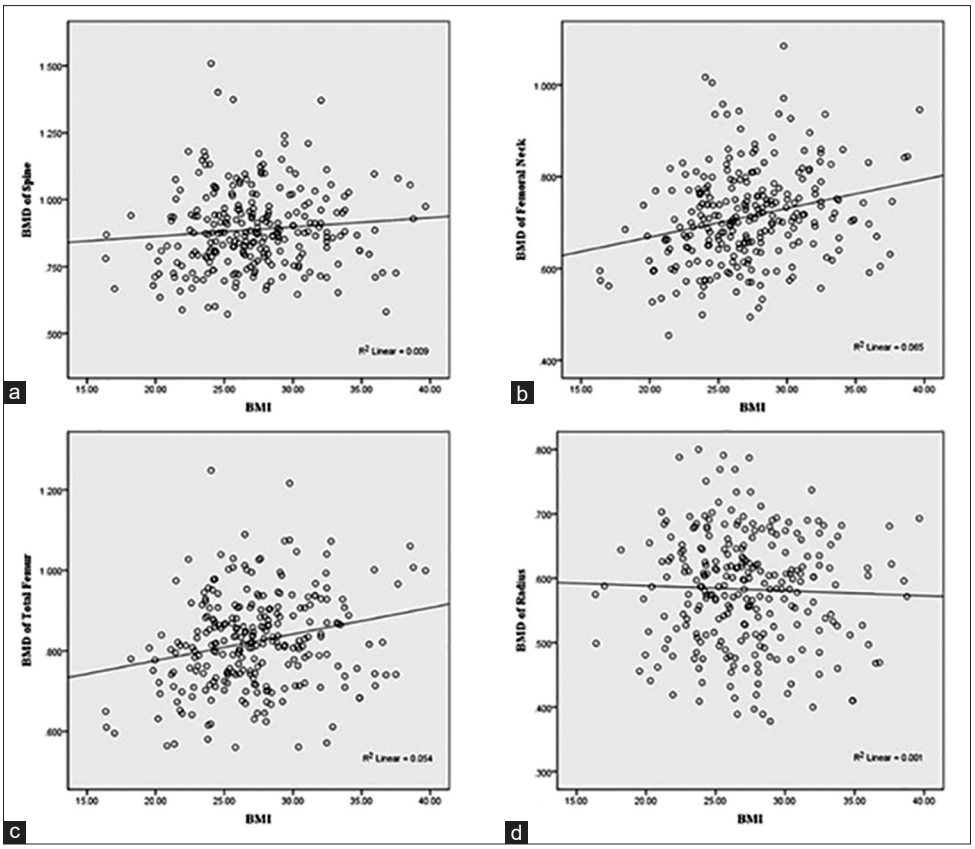

Figure 1: Scatterplots of correlation of bone mineral density of spine (a), femoral neck (b), total femur (c) and radius (d) versus body mass index. Pearson correlation between body mass index and bone mineral density of femoral neck, bone mineral density of total femur were statistically significant compared to bone mineral density of radius ($P < 0.000$) and ($P < 0.000$), ($P = 0.550$), respectively

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Conflicts of interest

There are no conflicts of interest.

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