BONE MINERAL DENSITY DISCORDANCES IN FEMALES: A COMPARISON OF PREMENOPAUSAL AND NON-GERIATRIC POSTMENOPAUSAL ADULT POPULATIONS

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ABSTRACT

Introduction*: Bone mineral density (BMD) discordance between lumbar and femoral T-scores can cause difficulties in the interpretation of dual x-ray absorptiometry (DXA) results. We aimed to compare BMD discordance in premenopausal and non-geriatric (early) postmenopausal women.*

Materials and methods*: Lumbar spine (L1-4) and femoral neck BMD measurements of premenopausal (n = 236/944) and postmenopausal (n = 708/944) women were performed by DXA. For both groups the mean age, BMD, T-scores, BMI, osteopenia-osteoporosis rates, concordance-discordance rates and the rates of the regions with lower T-scores were obtained and compared.*

Results*: Osteopenia and osteoporosis were more frequent in postmenopausal women than in premenopausal women (P < 0.05). Minor discordance rates were 26.3% (n = 62/236) in premenopausal women and 42.4% (n = 300/708) in postmenopausal ones (P < 0.05), whereas major discordance rates were 0% (n = 0/236) and 2.5% (n = 18/708), respectively (P < 0.05). In discordant cases of postmenopausal group, the rate of lumbar regions with lower T-scores was statistically higher than those of premenopausal group (P < 0.05). The majority (63.5%, n = 202/318) of postmenopausal women with T-score discordances had lower lumbar T-scores.*

Conclusion*: Because of higher prevalence of discordance in non-geriatric postmenopausal women, we recommend together lumbar and femoral BMD measurements for the diagnosis of osteopenia and osteoporosis.*

Keywords*:Bone Density, Femur Neck, Lumbar Vertebrae, Postmenopause.*

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Introduction

Osteoporosis without accompanying osteomalacia was defined as a decrease in bone mass without an identifiable change in the ratio of calcified to uncalcified matrix in which the disturbed microarchitecture causes increased bone fragility[1]. Bones become more fragile if the critical balance between osteoclastic resorption and osteoblastic build-up of bones is disturbed in favour of resorption[2]. Osteoporosis is a growing, worldwide health problem which affects both women and men[3-8]. Osteopenia is another important term used to define bone loss and refers to abnormal bone density which is not as low as osteoporosis[9]. Currently the diagnosis of osteopenia and osteoporosis is mainly performed by measuring bone mineral density (BMD) with dual x-ray absorptiometry (DXA)[3-5,8,10,11] which was widely accepted as the gold standard method[10,12,13]. However, discordance between lumbar and femoral T-scores can cause diagnostic dilemmas during interpretation of the BMD results and remains to be one of the main problematic issues of DXA measurements from the point of

diagnosis and treatment. Though in some studies the frequency of lumbar and femoral T-score discordance was reported to be as high as 41.6-51.15% among adult women[8,14,15], researches comparing the discordance rates of non-geriatric (early) postmenopausal women with those of premenopausal women were rarely be performed. Being aware of the rates of T-score discordance in non-geriatric postmenopausal women will lead the physician to properly obtain and evaluate both lumbar and femoral neck BMD measurements for an early start of preventive anti-osteoporotic treatment, in order to overcome the negative and rapid effect of the early period of menopause on BMD of particularly the lumbar vertebrae. In our cross-sectional study, we primarily aimed to compare BMD discordance rates in premenopausal and non-geriatric postmenopausal women in order to present statistically reliable daddy about this rarely investigated issue using a large sample size, and to evaluate the effect of menopause on T-score discordance. Besides, we also compared the rates of osteopenia and osteoporosis according to lumbar and femoral T-scores in both female groups.

Materials and methods

In this cross-sectional retrospective study between May 2011 and December 2011, totally 1246 consecutive outpatient non-geriatric adult females who readily underwent routine BMD measurements, who had no risk factors which could affect bone density (collagen tissue diseases, diabetes mellitus, history of salpingo-oophorectomy, premature menopause, etc.) and who were not on any medications that could affect bone metabolism (heparin, corticosteroids, vitamin D, estrogen, calcium, anticonvulsant drugs, thiazides, etc.) were recruited in the first selection by evaluating the records obtained from face-to-face interviews. The women in the geriatric age group (≥ 65 years) were not included in order to minimize the effect of late (senile) phase of bone loss on discordance. The subjects carrying metallic implants in their lumbar vertebrae and/or hips (n = 9) and the ones with insufficient or uncertain data about their menopausal status and medical history including the drugs used (n = 293), were excluded. The rest of the adult females (n = 944) were divided into two groups according to their menopausal status: The premenopausal group (n = 236) included women with regular menstruation, and the non-geriatric postmenopausal group (n = 708) included women who had amenorrhea for one year or more[16]. In the present study we retrospectively evaluated the lumbar and femoral neck DXA results of the included patients, which were obtained in accordance with institutional ethical guidelines. The study conformed to the World Medical Association Declaration of Helsinki (revised in 2000, Edinburgh).

In our daily DXA practice all the subjects have routinely been informed about BMD measurements and consent have been obtained from them. The mean ages of the subjects with standard deviations (SDs) in the whole study group, premenopausal group and non-geriatric postmenopausal group were 52.17 ± 6.39, 46.25 ± 4.24 and 54.14 ± 5.74 years, respectively. Mean duration of menopause with SD in non-geriatric postmenopausal group was 6.71 ± 4.82 years. We obtained height and weight of the subjects just before BMD measurements, and calculated body mass index (BMI) as: weight (kg)/height (m)^2[17]. The mean BMI of the whole study group was 30.96 ± 5.44 kg/m^2.The BMD measurements of lumbar spine (L1-4) and femoral neck in each subject were performed by a DXA device (Lunar Prodigy Advance; GE Medical Systems-Lunar, Madison, WI, USA). The T-scores (standard deviation of healthy young- adult mean) of the subjects were used to evaluate their BMD status[18]. According to the classification system proposed by The World Health Organization (WHO), the subjects were defined as normal with a T score ≥ -1.0, osteopenic with a T-score between -2.5 and -1, and osteoporotic with a T-score ≤ -2.5[1].

In both premenopausal and non-geriatric postmenopausal groups, concordance and discordance between lumbar and femoral neck T-scores were evaluated and compared. Concordance was defined as the presence of lumbar and femoral neck T-scores within the same normal, osteopenic or osteoporotic WHO class. Minor discordance was defined as the presence of only a single WHO class difference between lumbar and femoral neck T-scores. Obtaining osteoporotic T-scores in one lumbar or femoral neck region while getting normal T-scores in the other region was defined as major discordance[5,15].

Statistical analysis

For all the quantitative variables, mean values with SDs were given. The independent t-test was used to compare the mean age, BMD, T-scores and

BMI of premenopausal and non-geriatric postmenopausal groups. The frequencies of osteoporosis and osteopenia in lumbar and femoral neck regions according to T-scores were given as percentages. Chi-square test was used to compare osteopenia-osteoporosis rates, concordance-discordance rates and the rates of the regions with lower T-scores in premenopausal and non-geriatric postmenopausal women. P-values < 0.05 were considered as statistically significant. All analyses were done with SPSS software (version 16.0: SPSS Inc, Chicago, IL).

Results

The mean age of non-geriatric postmenopausal group was significantly higher than those of the premenopausal group (P < 0.05). There was no statistically significant difference between the mean BMI values of premenopausal and non-geriatric postmenopausal groups (P = 0.113). The mean BMD measurements of non-geriatric postmenopausal group were significantly lower than those of the premenopausal group (P < 0.05) (Table 1).

	Premenopausal group (n = 236)	**Non-geriatric postmenopausal group (n = 708)**	**P-value***
L1-4 (g/cm²)	1.147 ± 0.136	1.029 ± 0.154	0.000
L1-4 (T-score)	-0.37 ± 1.10	-1.31 ± 1.21	0.000
Femur neck (g/cm²)	0.947 ± 0.166	0.867 ± 0.130	0.000
Femur neck (T-score)	-0.57 ± 0.86	-1.22 ± 0.89	0.000
BMI (kg/m²)	30.48 ± 5.21	31.13 ± 5.51	0.113
Age (years)	46.25 ± 4.24	54.14 ± 5.74	0.000

Table 1: The mean BMD measurements, BMI and ages with standard deviations in premenopausal and non-geriatric postmenopausal groups.
**P-values < 0.05 are considered as statistically significant. BMD: Bone mineral density; BMI: Body mass index*

According to both lumbar and femoral neck BMD measurements, osteopenia and osteoporosis were more frequent in non-geriatric postmenopausal women than in premenopausal women (P < 0.05). Osteopenia and osteoporosis rates according to T-scores of lumbar and femoral neck regions in both premenopausal and non-geriatric postmenopausal groups were given in Table 2.

In the whole study group (n = 944), the rates of concordance, total discordance, minor discordance and major discordance were 59.7% (n = 564/944), 40.3% (n = 380/944), 38.3% (n = 362/944) and 1.9% (n = 18/944), respectively. Concordance was significantly more frequent in premenopausal women than in non-geriatric postmenopausal women (P < 0.05). Minor and major discordances were significantly more frequent in non-geriatric postmenopausal women than in premenopausal women (P < 0.05) (Table 3).

With regard to total cases with discordance in non-geriatric postmenopausal group, the rate of lumbar regions with lower T-scores was statistically higher than those of premenopausal group (P < 0.05). The majority (63.5%, n = 202/318) of non-geriatric postmenopausal women with T-score discordances had lower lumbar T-scores (Table 4).

Besides the percentages of the regions which had lower T-scores in minor and major discordances, the distribution of T-score concordances and discordances are also given for both premenopausal and non-geriatric postmenopausal women in Table 5.

Discussion

Since the frequency of osteoporosis-related fractures especially in postmenopausal women seems to increase in today's aging population[19], correct interpretation of DXA results and diagnosis of osteoporosis is very important.

	T-score category of L1-4 in premenopausal group (%, n)	**T-score category of L1-4 in non-geriatric postmenopausal group (%, n)**	**P-value***	**T-score category of femoral neck in premenopausal group (%, n)**	**T-score category of femoral neck in non-geriatric postmenopausal group (%, n)**	**P-value***
Osteopenia (-1.0 >T-score >-2.5)	30.50% (n = 72/236)	42% (n = 298/708)	0.000	30.50% (n = 72/236)	54.20% (n = 384/708)	0.000
Osteoporosis T-score ≤ -2.5	0.80% (n = 2/236)	19.60% (n = 139/708)	0.000	0.80% (n = 2/236)	6.90% (n = 49/708)	0.000

Table 2: The frequencies of the patients with osteopenia and osteoporosis in premenopausal and non-geriatric postmenopausal groups, according to T-scores of L1-4 and femoral neck.
**P-values < 0.05 are considered as statistically significant.*

	Premenopausal group (n=236)	Non-geriatric postmenopausal group (n=708)	P-value*
Concordance	73.7% (n = 174/236)	55.1% (n = 390/708)	0.000
Total Discordance	26.3% (n = 62/236)	44.9% (n = 318/708)	0.000
Minor Discordance	26.3% (n = 62/236)	42.4% (n = 300/708)	0.000
Major Discordance	0% (n = 0/236)	2.5% (n = 18/708)	0.000

Table 3: The frequencies of concordances and total, minor, major discordances given for premenopausal and non-geriatric postmenopausal groups.
**P-values < 0.05 are considered as statistically significant.*

Regions with lower T-scores	Total discordance in premenopausal group (n = 62/236)	Total discordance in non-geriatric postmenopausal group (n = 318/708)	P-value*
L1-4	50% (n = 31/62)	63.50% (n = 202/318)	0.046
Femoral neck	50% (n = 31/62)	36.50% (n = 116/318)	0.046

Table 4: The percentages of the regions with lower T-scores in total discordance given for premenopausal and non-geriatric postmenopausal groups.
**P-values < 0.05 are considered as statistically significant.*

Regions with lower T-scores	Premenopausal group (n = 236)		Non-geriatric postmenopausal group (n = 708)	
	Minor discordance (n = 62)	Major discordance (n = 0)	Minor discordance (n = 300)	Major discordance (n = 18)
L1-4	50% (n = 31/62)	0% (n = 0)	64% (n = 192/300)	55.60% (n = 10/18)
Femoral neck	50% (n = 31/62)	0% (n = 0)	36% (n = 108/300)	44.40% (n = 8/18)

Table 5a: The percentages of the regions with lower T-scores in minor and major discordance given for premenopausal and non-geriatric postmenopausal groups.

Postmenopausal women are particularly at increased risk for osteoporosis since bone loss in these subjects can be as high as 3-5% per year[6]. In a large-scale study including 246 premenopausal and 479 postmenopausal women, a significant decrease in BMD at the AP lumbar vertebrae and femoral neck could not be found in premenopausal women, whereas apparent bone loss in these regions, and a negative correlation between these regions and the years after menopause was detected in postmenopausal women[20].

In our study, the mean lumbar and femoral neck BMD measurements of non-geriatric early postmenopausal group were significantly lower than those of the premenopausal group which referred to much higher rate of osteopenia and

	Premenopausal group (n = 236)	Non-geriatric postmenopausal group (n = 708)	Total (n = 944)
T-score concordance	73.70% (n = 174/236)	55.10% (n = 390/708)	59.70% (n = 564/944)
Femoral neck and L1-4 normal	75.90% (n = 132/174)	45.10% (n = 176/390)	32.62% (n = 308/564)
Femoral neck and L1-4 osteopenia	23.50% (n = 41/174)	49% (n = 191/390)	24.60% (n = 232/944)
Femoral neck and L1-4 osteoporosis	0.60% (n = 1/174)	6.10% (n = 24/390)	2.60% (n = 25/944)
Major T-score discordance	0% (n = 0/236)	2.50% (n = 18/708)	1.90% (n = 18/944)
Femoral neck osteoporosis, L1-4 normal	0%	44.40% (n = 8/18)	0.84% (n = 8/944)
Femoral neck normal, L1-4 osteoporosis	0%	55.60% (n = 10/18)	1% (n = 10/944)
Minor T-score discordance	26.30% (n = 62/236)	42.40% (n = 300/708)	38.30% (n = 362/944)
Femoral neck osteoporosis, L1-4 osteopenia	1.60% (n = 1/62)	5.70% (n = 17/300)	1.90% (n = 18/944)
Femoral neck osteopenia, L1-4 osteoporosis	1.60% (n = 1/62)	35% (n = 105/300)	11.20% (n = 106/944)
Femoral neck osteopenia, L1-4 normal	48.40% (n = 30/62)	29.30% (n = 88/300)	12.50% (n = 118/944)
Femoral neck normal, L1-4 osteopenia	48.40% (n = 30/62)	30% (n = 90/300)	12.70% (n = 120/944)

Table 5b: The distribution of T-score concordances, major and minor discordances according to the classification system proposed by WHO* in premenopausal and non-geriatric postmenopausal groups.
**WHO: The World Health Organization*

osteoporosis in postmenopausal women. If we consider the relatively short mean duration of menopause in our postmenopausal patients (6.71 ± 4.82 years), it is obvious that dramatic changes in bone density occur in favour of osteopenia and osteoporosis shortly after menopause. In various studies the rate of lumbar and femoral osteoporosis in early postmenopausal period was given as 14.7-25.4% and 2.2-4.9%, respectively[8,21-23]. Also the rate of lumbar and femoral osteopenia in early postmenopausal period was reported as 28.1–38% and 32.7-45.8%, respectively[21,23]. In our non-geriatric postmenopausal group, the rates of osteoporosis and osteopenia in lumbar and femoral regions were similar or close to those obtained in the above mentioned studies.

In various studies, minor and major discordance rates in adult women were reported as 39-42% and 2.8-5%, respectively[14,15,24]. Discordance rates in our whole study group were close to those of above mentioned studies and it can be concluded that discordance was present in four of every 10 patients in our study.

Various patient-related causes such as age[8,14,15], menopause and obesity[14,15] were reported to be significantly associated with T-score discordance in women. Subgrouping the adult women as premenopausal and non-geriatric postmenopausal groups, and their comparison can reveal significant differences between their discordance rates. In a study including 3848 females, the percentage of postmenopausal women with discordance (46.9%) was significantly higher than that of premenopausal women (36.8%)[15].

In the above mentioned study[15] and in another large-scale study including 2871 adult women[14], the participants with discordance had also significantly higher mean age. Similarly in our study, non-geriatric postmenopausal women who were also older than premenopausal women had significantly higher minor and major discordance rates which led us consider that both age and menopause increased the rate of discordance. Obesity was described as having a BMI more than 30 kg/m^2 and it was accepted as a risk factor for major T-score discordance[14,15]. In our study the effect of obesity on the statistical difference between the rates of major discordance in both groups was considered to be minimal, because there was no significant difference between the mean BMI values of premenopausal and non-geriatric postmenopausal groups which were calculated as 30.48 ± 5.21 kg/m^2 and 31.13 ± 5.51 kg/m^2 (P = 0.113), respectively.

We evaluated the factors which played role in predominance of bone loss in lumbar vertebrae during postmenopausal period. Before menopause bone loss is not fast due to slow remodeling, but at menopause bone loss gets faster as the result of increase in the rate of remodeling[25]. Accelerated bone loss is prominent in the first decade of postmenopausal period and throughout this early phase, trabecular (cancellous) bone loss is three to five folds more than cortical bone loss which may lead to vertebral compression fractures[25,26]. Accelerated and disproportionate loss of trabecular bone in postmenopausal osteoporosis which occur in bones like vertebrae, was explained by increased resorption of bone despite insufficient formation[27,28], in which estrogen deficiency was thought to play a major role[28-31].

After the accelerated phase, late phase with slow bone loss which will continue through rest of the life predominates, affecting both trabecular and cortical bone[26]. This "senile bone loss" is thought to develop due to decrease in calcium absorption, deficiency in vitamin D, secondary hyperparathyroidism, deficiency of skeletal growth factors and other essential regulators in geriatric age group[26,29,30,32,33], though estrogen deficiency was also considered as an important etiology[20,29,31]. Furthermore, women have lower trabecular bone volume fraction and trabecular number compared to men, which can be an accelerating factor for trabecular bone loss in aging women[34]. It is important to differentiate these phases of osteoporosis and understand their mechanisms in order to make a proper treatment planning and to better understand T-score discordance. In a large-scale study with a mean female age of 53.8 years which included significantly high number of postmenopausal women with discordance (46.9%) compared to premenopausal women with discordance (36.8%), lower lumbar BMD was a more frequent finding in subjects with minor and major T-score discordances[15].

In another study including adult women with a mean age of 58.5 years which refers to predominantly the postmenopausal period, most subjects with discordance showed lower lumbar BMD (73.1%) compared to femoral BMD[35]. Similarly in our study, the majority (63.5%) of the postmenopausal women with both minor and major T-score discordances had lower lumbar BMD, and also the rate of lumbar regions with lower T-scores within the discordant cases of non-geriatric postmenopausal group was statistically higher than that of the premenopausal group. However, as it can be seen in Table 5 that the rate of the lumbar and femoral neck regions with lower T-scores among discordant cases in premenopausal group are equal (50%). It was also demonstrated in Table 2 that there is equal number of lumbar and femoral neck regions with both osteopenia and osteoporosis in premenopausal group. In the highlight of these data we consider that our cases with osteopenia and osteoporosis in premenopausal period had a tendency for even distribution of bone loss without any regional preference.

Also, it was interesting to see that even a single case of major discordance among premenopausal cases could not be detected despite the large sample size of this group. For the presence of major discordance, there should be osteoporosis in one lumbar or femoral neck region while getting normal T-scores in the other region, as mentioned above. In premenopausal group, the rate of osteoporosis was very low (0.8%) for each region.

Furthermore, the rates of lumbar and femoral neck regions with lower T-scores are equal in this group, as mentioned above. We suggest that low risk of osteoporosis and the absence of any demonstrable regional predominance of bone loss in premenopausal group prevented the occurrence of major discordance. In a study including geriatric women and postmenopausal non-geriatric women with mean age of 70.3 and 53.9 years respectively, the rate of osteoporosis was more than two folds in geriatric women compared to postmenopausal non-geriatric women[29]. Late, slow phase of osteoporosis could have interfered with accelerated, early postmenopausal osteoporosis in our study, but since the mean age of our postmenopausal subjects was less than 65 years and mean duration of menopause was 6.71 ± 4.82 years, we considered that the contribution of late, slow phase of osteoporosis was minimal. Researchers have also studied the positive effects of weight-bearing on bone density[36,37]. Because the femoral regions carry more weight than the lumbar vertebrae do, weight-bearing could have caused a relatively higher or more preserved femoral BMD of our patients in both groups. But since there was no significant difference between the mean BMI values of our premenopausal and non-geriatric postmenopausal groups, the effect of weight on the statistical difference between the rates of discordance in both groups was thought to be neutralized or minimal. Other common causes of patient-related discordance are spondylotic changes, calcifications of aorta, coxarthrosis, superimposed metallic objects or implants[15,20]. Besides patient-related reasons, the factors which could affect the performance of DXA measurements such as improper patient positioning can also cause T-score discordance[11,15]. In our study, assignment of different DXA operators during our study period could have caused technical T-score discordances in some BMD measurements. But since we had a standard DXA protocol, interoperator variability was considered to be minimal.

Since lumbar and femoral T-score discordance is a common finding which may lead to diagnostic difficulties while evaluating BMD results of perimenopausal and postmenopausal women, being aware of this entity is of utmost significance in diagnosis and treatment of osteoporosis[15,38]. In a large-scale BMD study with perimenopausal women, it was reported that referring to both lumbar and femoral T-scores increased the rate of osteoporosis by 50% or more[38]. In a more recent study, referring to the lowest T-scores increased the rate of osteoporosis from 4.03% to 10.75% in postmenopausal women because of lumbar and femoral T-score discordance[39]. It is also clear from our findings that we could have overlooked osteopenia or osteoporosis in either lumbar or femoral regions of the patients with discordance if we had not performed BMD measurements of both regions at the same setting. The diagnosis of osteoporosis has already been made by performing both lumbar and femoral BMD measurements[40]. Because of high prevalence of discordance, many other researchers also recommend a combination lumbar and femoral BMD measurements instead of measuring a single region in diagnosis of osteoporosis[5,15]. In subjects with minor or major discordance, the region with the lower T-score was recommended to be taken into consideration for the diagnosis of osteopenia or osteoporosis[5,14].

We had some limitations in our study mostly due to its retrospective design. Firstly, we could not exclude the patients with calcifications of abdominal aorta, vertebral osteoarthritis, hip osteoarthritis and/or scoliosis because we could not obtain additional radiological imaging of the subjects in the study group. This could have impact on T-score discordance in some patients. Secondly, we could not compare our findings with those of male population since our study population included only the females. Thirdly, we could not utilize the Fracture Risk Assessment Tool (FRAX®) to determine the 10-year probability of osteoporotic fracture risk of the patients[7] which was particularly important for the ones with osteoporosis and T-score discordance. Furthermore, we could not follow our patients to obtain the prevalence of osteoporotic fractures. However, the large number of cases in our study allowed us to confidently evaluate the effect of menopause on T-score discordance with a high statistical power. And finally, though our study provided a reliable daddybase with normative values, it is clear that more epidemiological studies with larger groups are needed for performing latent class analyses and principal component analyses in the future.

In conclusion, the majority of non-geriatric postmenopausal women with both minor and major T-score discordances had lower lumbar T-scores. Because of the high prevalence of discordance especially in the non-geriatric postmenopausal women, both lumbar and femoral BMD measurements are necessary in the diagnosis of osteopenia and osteoporosis.

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