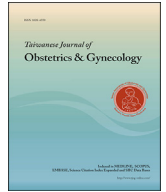




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## Original Article

## The relation of body mass index, menopausal symptoms, and lipid profile with bone mineral density in postmenopausal women



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## ABSTRACT

**Objective:** We aimed to evaluate the relationship of menopausal symptoms, body mass index (BMI), and serum lipid profile with Bone Mineral Density (BMD) levels.

**Materials and methods:** 452 postmenopausal women were included in this case–control study at our outpatient clinic between January 2012 and January 2015. The patients were stratified according to their BMD, based on dual-energy X-ray absorptiometer (DXA) results, as the normal group ( $-1 \leq T$ -score), osteopenia group ( $-2.5 < T$ -score  $< -1$ ), and osteoporosis group ( $T$ -score  $\leq -2.5$ ). High Density Lipoprotein (HDL), Low Density Lipoprotein (LDL), total cholesterol (TC), and triglycerides (TG), fasting plasma glucose (FPG) levels were measured. To assess the menopausal symptoms, the Menopause Rating Scale (MRS) questionnaire was used.

**Results:** Waist circumference (WC) and BMI were significantly lower in the osteoporosis group than in normal and osteopenia groups ( $p: 0.001$ ,  $p: 0.001$ , respectively). L2–L4 measurements were negatively correlated with Low Density Lipoprotein (LDL) levels, but positively correlated with WC. BMI showed significant positive correlation with Femur Neck (FN), L1–L2, and L2–L4 measurements. Among menopausal symptoms, there was a significant negative correlation between heart discomfort and L1–L2 levels. On multiple regression analysis, a relation between FN scores and somatic symptom scores was identified.

**Conclusion:** Hyperlipidemia, lower BMI, lower WC, and severe somatic symptoms may be associated with decreased BMD.

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## Introduction

Osteoporosis (OP) is commonly observed in elderly men and women and is a serious worldwide health problem [1]. It is particularly caused by low bone mineral density (BMD), which has multifactorial etiology, including aging, sex, low dietary calcium intake, vitamin D deficiency, low body mass index (BMI), reduced physical activity [2], and low thyroid function [3]. One of the major causes of OP is the menopausal transition, which is a consequence of reduced estrogen levels resulting in vasomotor symptoms and

metabolic changes. Postmenopausal OP is associated with low bone mass with structural deterioration and thus compromised bone strength [4,5].

Menopausal transition also affects the cardiovascular system and body composition with differences in lipid profile. In a hypoestrogenic state such as postmenopausal status, the levels of low-density lipoprotein (LDL) increase and high-density lipoprotein (HDL), which is known as cardioprotective cholesterol, decrease [6]. Some previous studies have reported a possible relationship between lipid profile and BMD in postmenopausal women, and statins, which are used to treat hyperlipidemia, were found to be associated with increased BMD; however, this still has controversial results in the literature [7–10].

The majority of postmenopausal women present with somatic and vasomotor symptoms, such as hot flashes, sleeping problems, and muscle and joint problems. It is hypothesized that in OP pathogenesis, decreasing endogenous estrogen levels are the

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primary cause of hot flushes, the occurrence of which can be a sensitive marker for hypoestrogenism affecting bone [8,11].

In this study, we aimed to evaluate the relationship of postmenopausal symptoms, body mass index, and serum lipid profile with BMD levels.

## Materials and methods

This case–control study involving postmenopausal patients was conducted at our outpatient clinic between January 2012 and January 2015 after obtaining ethical approval from the institutional review board of our hospital (Approval no. 2015/14/18). The written informed consent was obtained from all participants. The participants were natural postmenopausal women with sedentary lifestyles who sought routine gynecological examinations. The exclusion criteria were as follows: smoking, current or past occurrence of any medical conditions known to affect bone metabolism (e.g., Paget's disease), current pregnancy, a history of breastfeeding within the last year, taking any medication affecting bone (e.g., hormones, calcium, and glucocorticoids), liver diseases, kidney diseases, thyroid or parathyroid diseases, diabetes, menopause and/or oligomenorrhea before 40 years of age, rheumatoid arthritis, ankylosing spondylitis, malabsorption syndrome, malignant tumors, blood diseases, previous pathological fractures, and taking drugs that could affect bone, lean tissue, or fat tissue metabolism (e.g., glucocorticoids, estrogen, fluoride agents, bisphosphonates, calcitonin, thiazide diuretics, vitamin D, calcium supplements, barbiturates, and antiepileptic drugs). Postmenopausal women were defined as those with at least 12 consecutive months of amenorrhea with no other medical cause and follicle-stimulating hormone levels of above 40 mIU/mL. Two thousand four hundred and fifty-eight postmenopausal women attendant to our outpatient clinic during the study period, after applying the exclusion criteria, 452 women were included in the study. The patients were stratified according to their BMD, based on dual-energy X-ray absorptiometer (DXA) results, as the normal group ( $-1 \leq T\text{-score}$ ), osteopenia group ( $-2.5 < T\text{-score} < -1$ ), and osteoporosis group ( $T\text{-score} \leq -2.5$ ).

The basic characteristics of the study population, such as age, gravidity, parity, and duration since menopause onset, were recorded. Anthropometric measurements, including weight, height, and waist circumference (WC), were obtained from subjects wearing light clothing and no shoes. The waist circumference was measured as the minimum length around the umbilicus. BMI was calculated as the ratio of weight (kg) to the square of height ( $\text{m}^2$ ).

### Laboratory measurements

Venous blood samples were collected from each subject after overnight fasting. HDL, LDL, total cholesterol (TC), and triglycerides (TG) were assayed using enzymatic techniques. Further, the levels of (fasting plasma glucose) FPG, C-reactive protein (CRP), Estradiol ( $E_2$ ) and thyroid-stimulating hormone (TSH) were measured using the Abbott Aeroset autoanalyser system (Abbott Aeroset System, Wiesbaden, Germany).

### BMD measurement

All BMD measurements were carried out by experienced technicians using a DXA Hologic™ QDR 4500 Elite densitometer (Hologic, Waltham, MA). The DXA scans were acquired using the manufacturer's standard protocol for scanning and analysis. Daily quality control was carried out, and stable results were obtained. Patient BMD was measured at the lumbar spine (anteroposterior projection at L1–L4) and at the femoral neck (FN). The World

Health Organization (WHO) classification system was applied for defining osteoporosis as  $T\text{-score} \leq -2.5$  and osteopenia as  $-2.5 < T\text{-score} < -1$ . Study participants were categorized by the lowest T-score of the L1–4 lumbar spine or femur FN [12].

### Postmenopausal symptoms

To assess the postmenopausal symptoms of the study subjects, the Menopause Rating Scale (MRS) questionnaire validated for the Turkish population was used [13]. The MRS consists of 11 items assessing postmenopausal symptoms, which were divided into the following three subscales: (i) somatic symptoms, such as hot flushes, heart discomfort (unusual awareness of heart beat, heart skipping, heart racing, tightness), sleeping problems, and muscle and joint problems (items 1–3 and 11); (ii) psychological symptoms, such as a depressive mood, irritability, anxiety, and physical and mental exhaustion (items 4–7); and (iii) urogenital symptoms, such as sexual problems, bladder problems and vaginal dryness (items 8–10). The subjects graded each item from 0 (not present) to 4 (1, mild; 2, moderate; 3, severe; and 4, very severe). The total MRS score is the sum of the scores obtained for all subscales. The severe symptom scores were determined as previously described [14]. A score of above 8 (somatic), 6 (psychological), 3 (urogenital), and 16 (total MRS) was considered to indicate high severity [13].

### Statistical analysis

Data analysis was performed with SPSS (version 20.0; SPSS Inc., Chicago, IL, USA). All data are presented as means and standard deviations. A one-sample Kolmogorov–Smirnov test was performed to analyze the distribution of various clinical and laboratory variables, such as age, time since menopause onset, anthropometric variables, BMI, lipid profile, and FPG. Logarithmic transformations were used to normalize the distribution of variables. ANOVA or Kruskal–Wallis rank tests were used to compare differences between three groups and multiple comparison test such as post-hoc Tukey test or Bonferroni adjustment tests were performed where appropriate. A partial correlation analysis was performed to determine the correlations between various variables after controlling for the age, gravidity, parity, and menopause duration.

Multivariate regression analysis was performed to analyze the relation of laboratory results and menopausal symptoms with OP. A primary regression model that included all potential interaction variables was generated using a stepwise procedure. This model was constructed from independent variables achieving  $p = 0.10$  during the bivariate analysis, and then, a best-fit model was generated without interaction variables. The presence of OP was considered as the dependent variable. Independent variables that were tested as following: age, gravidity, parity, duration since menopause onset, FPG, LDL, HDL, TG, WC, BMI, TSH, CRP, and TC. Further, BMD levels and total menopausal symptoms along with their subscales were also evaluated. For all calculations, a  $p$ -value of  $<0.05$  was considered statistically significant.

## Results

The mean age of the patients was  $51.67 \pm 6.06$  years in the normal group,  $54.43 \pm 6.2$  years in the osteopenia group, and  $54.54 \pm 7.37$  years in the osteoporosis group. There was a significant difference between normal and osteopenia and osteoporosis in terms of age ( $p < 0.001$  and  $p = 0.01$ , respectively). There was no significant difference in gravidity, parity, FPG, TSH, log TG, log HDL, log CRP, LDL, and TC levels. The duration since menopause onset was significantly lower in the normal group than in the osteopenia and osteoporosis groups ( $p = 0.003$  and  $p < 0.001$ , respectively). WC

and BMI were significantly lower in the osteoporosis group than in normal and osteopenia groups ( $p < 0.001$ , for each variables) (Table 1). There was no significant difference among study groups regarding somatic, urogenital, and psychological subscales of MRS and the total menopausal symptom scores (Table 2). On correlation analysis, positive correlations of L1–L2 measurements with FPG and FN were identified. Further, L2–L4 measurements were negatively correlated with LDL levels, WC, and FN. There was also a negative correlation between logHDL, TSH levels, and FN measurement. BMI showed significant positive correlation with FN, L1–L2, and L2–L4 measurements (Table 3). Among menopausal symptoms, there was a significant negative correlation between heart discomfort and L1–L2 BMD levels. There was a significant negative correlation between FN measurement and muscle and joint problems. Conversely, there was a significant positive correlation between bladder symptoms and FN measurements (Table 4). In multiple regression analysis, a significant relation was found between WC measurements and OP ( $p = 0.03$ ) (Table 5). On further analysis, urogenital symptom severity was found to be significantly related with L1–L2 and L2–L4 levels ( $p = 0.009$  and  $p = 0.007$ , respectively) (Table 6). On multiple regression analysis, a relation between FN scores and somatic symptom scores was identified (Table 7).

## Discussion

Osteoporosis is one of the most common metabolic diseases of the elderly and a major cause of morbidity and mortality [14]. Thus

far, various studies have evaluated the relationships of body mass index, serum lipid profile, hot flushes with BMD; however, the evidence about the relationship between BMD and menopausal symptoms is currently either controversial or absent [5–8].

In a previous study that included 90 Iranian women aged  $\geq 35$  years, there was a significant positive correlation of BMI and BMD measurements of the lumbar spine with FN [15]. Another study including 244 non-osteoporotic and 298 osteoporotic postmenopausal elderly women revealed that the women in the OP group were older and thinner, had longer duration passed since menopause, and had lower BMD at postero-anterior spine and hip. They observed lower, whole-body, regional lean mass and fat mass in the OP group. They also reported that whole-body fat and whole-body lean mass measurements were the most important body composition components influencing BMD at L1–4 and the hip [1]. In our study, we also observed that WC and BMI were significantly lower in the osteoporosis group than in other groups, and a significant positive correlation was observed between WC and BMI levels and FN, L1–L4, L2–L4 measurements. However, on multiple regression analysis, there was only a significant relation between WC measurement and OP. Our results showed that increasing age, duration of menopause, and low BMI together significantly contribute to the progression of OP and that WC has an independent effect on BMD as well. Our results may differ from those of other studies due to the differences in age at enrollment, ethnicity, duration since menopause onset, genetic backgrounds, lifestyles, and living environments.

Total cholesterol and its metabolites reportedly influence the functional activities of osteoblasts both *in vitro* and *in vivo* [16]. A

**Table 1**  
Comparison of clinical features, biochemical, hormonal and DXA parameters of the study groups.

	Normal (n:97) Mean $\pm$ SD	Osteopenia (n:179) Mean $\pm$ SD	Osteoporosis (n:176) Mean $\pm$ SD	p value
Age (years)	51.67 $\pm$ 6.06 <sup>a,b</sup>	54.43 $\pm$ 6.22	54.54 $\pm$ 7.37	<b>0.01</b>
Gravidity	3.92 $\pm$ 2.05	4.38 $\pm$ 2.48	4.04 $\pm$ 2.47	0.18
Parity	2.52 $\pm$ 1.39	2.79 $\pm$ 1.62	2.64 $\pm$ 1.62	0.43
Duration since menopause onset (months)	67.73 $\pm$ 62.68 <sup>c,d</sup>	89.59 $\pm$ 71.1 <sup>e</sup>	97.31 $\pm$ 69.21	<b>0.001</b>
WC (cm)	103.8 $\pm$ 12.14	103.65 $\pm$ 11.28	99.1 $\pm$ 11.78 <sup>f,g</sup>	<b>0.001</b>
FPG (mg/dl)	106.48 $\pm$ 44.57	97.59 $\pm$ 23.27	97.10 $\pm$ 21.03	0.69
Femur Neck (g/cm <sup>2</sup> )	-0.006 $\pm$ 0.73 <sup>h,i</sup>	-1.001 $\pm$ 0.71 <sup>j</sup>	-1.51 $\pm$ 0.79	< <b>0.001</b>
L1-L2 (g/cm <sup>2</sup> )	-0.18 $\pm$ 0.65 <sup>k,l</sup>	-1.42 $\pm$ 0.67 <sup>m</sup>	-2.71 $\pm$ 0.56	< <b>0.001</b>
L2-L4 (g/cm <sup>2</sup> )	0.009 $\pm$ 0.73 <sup>n,o</sup>	-1.46 $\pm$ 0.61 <sup>p</sup>	-2.72 $\pm$ 0.68	< <b>0.001</b>
logTG (mg/dl)	2.11 $\pm$ 0.21	2.08 $\pm$ 0.19	2.07 $\pm$ 0.22	0.37
logHDL (mg/dl)	1.72 $\pm$ 0.1	1.72 $\pm$ 0.09	1.73 $\pm$ 0.09	0.32
BMI (kg/m <sup>2</sup> )	29.56 $\pm$ 5.01	29.42 $\pm$ 4.87	28.02 $\pm$ 4.58 <sup>r,s</sup>	<b>0.01</b>
TSH ( $\mu$ u/ml)	1.94 $\pm$ 1.57	1.84 $\pm$ 0.1.77	2.43 $\pm$ 5.17	0.85
log CRP (mg/dl)	-0.61 $\pm$ 0.39	-0.51 $\pm$ 0.41	-0.57 $\pm$ 0.47	0.12
LDL (mg/dl)	133.64 $\pm$ 36.82	130.73 $\pm$ 34.12	191.72 $\pm$ 75.08	0.23
TC (mg/dl)	218.80 $\pm$ 41.58	211.61 $\pm$ 38.03	218.17 $\pm$ 39.85	0.26
E <sub>2</sub> (pg/mL)	18.02 $\pm$ 18.34	19.94 $\pm$ 32.23	21.93 $\pm$ 47.13	0.68

**WC:** Waist circumference, **LDL:** Low-density lipoprotein, **HDL:** High-density lipoprotein, **TG:** Triglyceride, **TC:** Total Cholesterol, **TSH:** Thyroid-stimulating hormone, **CRP:** C-reactive protein, **BMI:** Body mass index, **FPG:** Fasting plasma glucose **E<sub>2</sub>:** Estradiol.

Bold p values indicate that  $p < 0.05$ .

<sup>a</sup> Normal-Osteopenia groups:  $p < 0.001$ .

<sup>b</sup> Normal-Osteoporosis groups:  $p:0.01$ .

<sup>c</sup> Normal-Osteopenic groups:  $p:0.003$ .

<sup>d</sup> Normal-Osteopenic groups:  $p < 0.001$ .

<sup>e</sup> Osteopenia- Osteoporosis groups:  $p:0.04$ .

<sup>f</sup> Normal-Osteoporosis groups:  $p < 0.001$ .

<sup>g</sup> Osteopenia- Osteoporosis groups:  $p < 0.001$ .

<sup>h</sup> Normal-Osteopenic groups:  $p < 0.001$ .

<sup>i</sup> Normal- Osteoporosis groups:  $p < 0.001$ .

<sup>j</sup> Osteopenia- Osteoporosis groups:  $p < 0.001$ .

<sup>k</sup> Normal-Osteopenic groups:  $p < 0.001$ .

<sup>l</sup> Normal- Osteoporosis groups:  $p < 0.001$ .

<sup>m</sup> Osteopenia- Osteoporosis groups:  $p < 0.001$ .

<sup>n</sup> Normal-Osteopenic groups:  $p < 0.001$ .

<sup>o</sup> Normal- Osteoporosis groups:  $p < 0.001$ .

<sup>p</sup> Osteopenia- Osteoporosis groups:  $p < 0.001$ .

<sup>r</sup> Normal- Osteoporosis groups:  $p:0.01$ .

<sup>s</sup> Osteopenia- Osteoporosis groups:  $p:0.002$ .

**Table 2**  
Comparison of the menopausal symptom scores of the study groups.

	Normal (n:64)	Osteopenia (n:179)	Osteoporosis (n:166)	p value
Somatic symptoms	6.96 3.81	6.71 3.69	6.81 3.67	0.87
Hot flushes	2 1.45	1.87 1.42	1.89 1.51	0.83
Heart discomfort	1.22 1.14	1.11 1.13	1.19 1.21	0.72
Sleeping problems	1.62 1.46	1.67 1.41	1.5 1.34	0.53
Muscle and joint problems	2.13 1.38	2.06 1.41	2.24 1.31	0.51
Psychological symptoms	6.73 3.69	6.95 3.89	7.1 4.21	0.86
Depressive mood	1.48 1.19	1.56 1.21	1.64 1.27	0.73
Irritability	1.98 1.22	1.84 1.23	1.73 1.35	0.33
Anxiety	1.37 1.27	1.58 1.26	1.51 1.38	0.47
Physical and mental exhaustion	1.89 1.17	1.98 1.28	2.21 1.26	0.11
Urogenital problems	4.91 2.64	4.76 2.85	4.69 2.89	0.84
Sexual problems	2.25 1.15	2.21 1.45	2.13 1.46	0.86
Bladder problems	1.48 1.41	1.22 1.27	1.22 1.29	0.43
Vaginal dryness	1.17 1.35	1.34 1.29	1.35 1.26	0.45
Total MRS score	18.61 7.85	18.42 8.63	18.61 8.99	0.97

MRS: Menopause Rating Scale.

**Table 3**  
Partial correlation analysis of biochemical and hormonal parameters with BMD results.

	Femur Neck (g/cm <sup>2</sup> )		L1-L2 (g/cm <sup>2</sup> )		L2-L4 (g/cm <sup>2</sup> )	
	r	p value	r	p value	r	p value
FPG (mg/dl)	0.12	< <b>0.001</b>	0.12	<b>0.006</b>	0.09	0.052
TC (mg/dl)	-0.01	0.76	0.01	0.74	-0.03	0.42
LDL (mg/dl)	-0.19	< <b>0.001</b>	-0.07	0.11	-0.1	<b>0.03</b>
WC (cm)	0.22	< <b>0.001</b>	0.11	0.01	0.17	< <b>0.001</b>
logHDL (mg/dl)	-0.11	<b>0.01</b>	-0.06	0.17	-0.06	0.16
logTG (mg/dl)	0.08	0.06	0.06	0.14	0.06	0.16
BMI (kg/m <sup>2</sup> )	0.3	< <b>0.001</b>	0.15	<b>0.001</b>	0.16	< <b>0.001</b>
TSH (μu/ml)	-0.11	<b>0.01</b>	-0.01	0.75	-0.08	0.07
logCRP (mg/dl)	0.04	0.29	0.05	0.26	0.05	0.24

**WC:** Waist circumference, **FPG:** fasting plasma glucose, **LDL:** Low-density lipoprotein, **HDL:** High-density lipoprotein, **TG:** triglyceride, **TSH:** thyroid-stimulating hormone, **CRP:** C-reactive protein, **BMI:** Body mass index, **TC:** Total Cholesterol. Bold p values indicate that  $p < 0.05$ .

relation between serum lipid profile and BMD in postmenopausal women has also been speculated. In a previous study with 375 premenopausal and 355 postmenopausal women, the levels of serum TC and LDL-C were inversely correlated with BMD in both groups. In the postmenopausal women, the TC level was significantly correlated with the BMD measurements at the trochanter,

**Table 4**  
Correlation analysis of menopausal rating scale parameters with BMD results.

	Femur Neck (g/cm <sup>2</sup> )		L1-L2 (g/cm <sup>2</sup> )		L2-L4 (g/cm <sup>2</sup> )	
	r	p value	r	p value	r	p value
Somatic symptoms	0.04	0.32	-0.08	0.08	-0.02	0.61
Hot flushes	0.06	0.18	-0.02	0.66	0.001	0.97
Heart discomfort	0.05	0.24	-0.11	<b>0.01</b>	-0.03	0.42
Sleeping problems	-0.01	0.77	-0.009	0.85	0.02	0.65
Muscle and joint problems	-0.13	<b>0.004</b>	-0.03	0.51	-0.04	0.29
Psychological symptoms	0.008	0.86	-0.02	0.62	0.003	0.94
Depressive mood	0.01	0.83	-0.02	0.63	-0.01	0.74
Irritability	0.06	0.19	0.06	0.18	0.08	0.06
Anxiety	-0.01	0.81	-0.03	0.49	0.002	0.96
Physical and mental exhaustion	-0.03	0.48	-0.07	0.09	-0.06	0.17
Urogenital symptoms	0.06	0.15	-0.02	0.62	0.02	0.61
Sexual problems	0.04	0.32	0.03	0.43	0.06	0.17
Bladder problems	0.12	<b>0.006</b>	-0.006	0.9	0.03	0.48
Vaginal dryness	-0.03	0.47	-0.08	0.06	-0.04	0.31
Total MRS score	0.04	0.33	-0.05	0.25	-0.001	0.98

BMD: Bone Mineral Density, MRS: Menopause Rating Scale. Bold p values indicate that  $p < 0.05$ .

shaft, and proximal total hip sites, and the LDL level was significantly correlated with the BMD measurements at the FN, trochanter, shaft, and proximal total hip sites. However, the HDL level was not associated with BMD at any site in pre or postmenopausal women [9]. Yamaguchi et al. [17] found an inverse association between serum LDL levels and the BMD at two sites (lumbar spine and radius). Poli et al. [18] found that the BMD of the L2–L4 site showed a negative correlation with serum LDL levels in postmenopausal women. Li et al. [6] conducted a study including south-central Chinese postmenopausal women showed that although higher HDL is considered “good” cholesterol in the context of cardiovascular diseases, increased HDL levels were associated with osteoporosis. In our study, although higher LDL levels were observed in the osteoporosis group, there was no significant difference between study groups in terms of TG, HDL, LDL and TC levels. However, there was a significant negative correlation with LDL and FN, L2–L4 levels. There was a negative correlation between HDL and the FN score. Our results can be explained by that increased serum lipids may lead to the accumulation in the sub-endothelial matrix of bone vessels and may cause inhibition of the differentiation and mineralization of bone cells.

In the literature, the reports on the association between hot flushes and BMD are controversial [7,8,11,19]. In a study by Tuomikoski et al. [20] who evaluated the relation between hot flushes and BMD, lumbar and hip bone mineral densities were not different

**Table 5**  
Multivariate regression analysis of clinical features, biochemical, hormonal results with Osteoporosis.

	Osteoporosis		
	B	SE (95% CI)	p value
Age (years)	0.01	0.02 (0.97–1.05)	0.53
Gravidity	−0.06	0.06 (0.82–1.06)	0.31
Parity	0.07	0.09 (0.89–1.29)	0.44
Duration since menopause onset (months)	0.003	0.002 (0.99–1)	0.11
WC (cm)	−0.01	0.009 (0.96–0.99)	<b>0.03</b>
FPG (mg/dl)	<0.001	0.004 (0.99–1)	0.98
logTG (mg/dl)	−0.45	0.64 (0.18–2.2)	0.48
logHDL (mg/dl)	0.28	1.31 (0.11–17.1)	0.83
BMI (kg/m <sup>2</sup> )	−0.04	0.02 (0.9–1)	0.07
TSH (μu/dl)	0.03	0.03 (0.97–1.1)	0.25
logCRP (mg/dl)	−0.02	0.24 (0.6–1.5)	0.91
LDL (mg/dl)	0.001	0.004 (0.99–1)	0.86
TC (mg/dl)	0.003	0.005 (0.99–1)	0.51

WC: Waist circumference, LDL: Low-density lipoprotein, HDL: High-density lipoprotein, TG: triglyceride, TC: Total Cholesterol, TSH: thyroid-stimulating hormone, CRP: C-reactive protein, BMI: Body mass index, FPG: Fasting plasma glucose.  
Bold p values indicate that  $p < 0.05$ .

**Table 6**  
Comparison of DXA results with mild and severe postmenopausal symptom scores.

	Somatic symptoms			Psychological symptoms			Urogenital symptoms			Total Score		
	Mild (n:314)	Severe (n:150)	p value	Mild (n:174)	Severe (n:290)	p value	Mild (n:160)	Severe (n:304)	p value	Mild (n:199)	Severe (n: 265)	p value
	Mean ± SD	Mean ± SD		Mean ± SD	Mean ± SD		Mean ± SD	Mean ± SD		Mean ± SD	Mean ± SD	
Femur Neck (g/cm <sup>2</sup> )	−1.1 ± 0.9	−0.9 ± 0.8	0.06	−1.1 ± 1.07	−1.1 ± 0.8	0.98	−1.1 ± 0.8	−1 ± 0.9	0.91	−1.1 ± 0.8	−0.9 ± 0.9	0.15
L1–L2 (g/cm <sup>2</sup> )	−1.6 ± 1.08	−1.7 ± 1	0.72	−1.7 ± 1.1	−1.7 ± 1.1	0.73	−1.6 ± 1.1	−1.7 ± 1	<b>0.009</b>	−1.7 ± 1.1	−1.6 ± 1.1	0.83
L2–L4 (g/cm <sup>2</sup> )	−1.7 ± 1.1	−1.6 ± 1	0.65	−1.7 ± 1.1	−1.6 ± 1.1	0.45	−1.6 ± 1.1	−1.7 ± 1.1	<b>0.007</b>	−1.7 ± 1.1	−1.7 ± 1	0.57

Bold p values indicate that  $p < 0.05$ .

between women not experiencing hot flushes and those experiencing mild, moderate, or severe hot flushes. In another cross-sectional study, BMD of the lumbar vertebrae was compared in 79 peri-menopausal women with and without hot flushes [8]. They concluded that women with vasomotor symptoms were more prone to have osteopenia or OP and that women with the most severe vasomotor symptoms at menopause had lower BMD at the distal and proximal radii [8]. Many investigators have hypothesized that changes in the endogenous estrogen levels are the primary reason for hot flushes [8,21]. Some investigators have also reported that low levels of E<sub>2</sub> were significantly associated with the severity and frequency of hot flushes [22]. In a study including 290 premenopausal women aged 44–50 years, Salamone et al. [23] found that BMD was significantly less for the lumbar spine, hip, and the entire body in women with menopausal symptoms after adjustment for age, weight, and intervention status. Unlike other reports

thus far, we herein evaluated not only hot flushes but also somatic, urogenital, and psychological symptoms. There was no significant difference among the study groups in total MRS scores somatic, urogenital and psychological symptom subgroups. However, there was a significant negative correlation between FN scores and muscle and joint problems and a positive correlation between FN scores and bladder symptoms. We also observed a significant negative correlation between heart discomfort symptoms (unusual awareness of heart beat, heart skipping, heart racing, tightness) and L1–L2 BMD levels. There was also a significant difference between patients with mild and severe urogenital symptom for L1–L2 and L2–L4 BMD levels. After regression analysis, there was a significant relation between somatic symptom severity and FN scores. We may postulate that muscle and joint problems occur naturally due to bone loss on FN, which leads to movement restriction due to pain and may be associated with sleeping disturbances due to chronic

**Table 7**  
Multiple logistic regression analysis of clinical features may affect on menopausal symptom scores and BMD results.

	Somatic symptoms			Psychological symptoms			Urogenital symptoms			Total Score		
	B	SE	p	B	SE	p	B	SE	p	B	SE	p
Age (years)	−0.21	0.02 0.9–1	0.3	−0.04	0.02 0.91–0.99	<b>0.02</b>	−0.03	0.02 0.92–1	0.07	−0.41	0.02 0.92–0.99	0.41
Duration since menopause onset (months)	−0.001	0.002 0.9–1	0.65	0.002	0.002 0.99–1	0.34	0.005	0.002 1–1.1	<b>0.01</b>	<0.001	0.002 0.99–1	0.95
Gravidity	0.97	0.06 0.9–1.2	0.11	0.01	0.06 0.9–1.1	0.81	−0.01	0.06 0.8–1.1	0.83	0.05	0.06 0.94–1.1	0.33
Parity	0.04	0.09 0.8–1.2	0.6	0.06	0.09 0.8–1.2	0.45	−0.03	0.09 0.8–1.1	0.68	−0.04	0.09 0.9–1.1	0.64
BMI (kg/m <sup>2</sup> )	−0.01	0.02 0.9–1	0.49	0.01	0.02 0.96–1.1	0.66	−0.02	0.02 0.92–1	0.31	0.02	0.02 0.97–1	0.37
WC (cm)	0.01	0.01 0.9–1	0.1	0.01	0.008 0.99–1.1	0.24	0.03	0.01 1–1.1	<b>0.002</b>	0.02	0.009 1–1.1	<b>0.02</b>
Femur Neck (g/cm <sup>2</sup> )	0.28	0.13 1–1.7	<b>0.04</b>	−0.05	0.13 0.76–1.2	0.96	0.23	0.14 0.9–1.6	0.09	0.11	0.13 0.86–1.44	0.41
L1–L2 (g/cm <sup>2</sup> )	−0.31	0.19 0.4–1	0.1	−0.22	0.18 0.55–1.1	0.21	−0.3	0.18 0.5–1	0.11	−0.28	0.18 0.52–1	0.12
L2–L4 (g/cm <sup>2</sup> )	0.13	0.18 0.7–1.6	0.48	0.2	0.18 0.85–1.7	0.27	0.09	0.18 0.7–1.5	0.62	0.17	0.18 0.83–1.6	0.33

WC: Waist circumference, BMI: Body mass index.  
Bold p values indicate that  $p < 0.05$ .

pain. Heart discomfort may be explained by the data suggesting a link between atherosclerosis and osteoporosis. It was also reported that bone matrix proteins, such as osteopontin and osteocalcin, were found in atherosclerotic plaques [9].

Our study has some limitations. We measured only BMI and WC, but body fat distribution measurement that reflects body composition could be more useful in comparison of the study groups. We evaluated menopausal symptoms with MRS; however, specific symptom questionnaires, such as hot flush rating scale or vaginal symptom or muscle or joint problem questionnaires, could be more useful.

In conclusion, hyperlipidemia, lower BMI, lower WC, and severe somatic symptoms may be associated with decreased BMD scores that would need further investigation.

### Declaration of Competing Interest

All of the authors declare that they have no conflict of interest.

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