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Original Research

Urogenital Symptoms are Associated With Bone Mineral Density but not With Metabolic Syndrome in Postmenopausal Women: A Prospective Cross-Sectional Study

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Abstract

Background: Menopause imposes a significant physical and emotional burden on women, affecting their quality of life and overall health. Beyond these challenges, the decline in estrogen levels during menopause is closely associated with adverse changes in bone health and an increased risk of developing metabolic syndrome (MetS), both of which contribute to long-term morbidity. The primary hypothesis of the current study was that the co-existence of low bone mineral density (BMD) and MetS would exacerbate the severity of menopausal symptoms. As the most bothersome menopausal symptoms typically emerge one year before the final menstrual period and gradually subside thereafter, we investigated BMD, MetS, and menopause-related symptoms in postmenopausal women within 10 years of menopause onset. **Methods**: A total of 193 postmenopausal women were included in this cross-sectional study, which was conducted at a university hospital in Istanbul. At baseline, participants were categorized into MetS and non-MetS groups based on the National Cholesterol Education Program-Adult Treatment Panel III (NCEP-ATP III) criteria. For comparative analyses, participants were stratified according to MetS status and BMD. Women with osteopenia or osteoporosis based on BMD measurements were combined into the low BMD group. Menopausal symptoms were assessed using the Menopause Rating Scale (MRS). **Results**: Women with MetS were significantly older and had a longer duration of menopause than those without MetS. All MRS scores were comparable between the MetS and non-MetS groups. Women with low BMD were older, had a longer duration of menopause, and a lower body mass index (BMI) compared to those with normal BMD. The MRS urogenital symptom subscale score was significantly higher among women with low BMD ($p = 0.019$). Severe urogenital symptoms were observed among women with co-existence of MetS and low BMD. Correlation analyses between MRS scores and other variables yielded negligible negative correlations with age. **Conclusions**: Low BMD was associated with higher scores on the urogenital subscale of the MRS, whereas MetS showed no significant relationship with menopausal symptoms. Women with both low BMD and MetS experienced more severe urogenital symptoms.

Keywords: menopause; bone mineral density; metabolic syndrome; urogenital symptoms

1. Introduction

Menopause is a physiological milestone that signifies the cessation of menstrual cycles and the end of reproductive capacity in women [1]. It typically occurs between the ages of 45 and 55 and is primarily caused by decreased production of estrogen and progesterone hormones [1]. This is a major period in terms of women's health with effects that extend far beyond reproductive function [1,2]. Vasomotor symptoms 80% and vulvovaginal symptoms demonstrate a 34% prevalence among postmenopausal women [3]. The steep decline in estrogen levels has many multisystemic consequences that can also lead to alterations in metabolic syndrome (MetS) components, such as lipid profiles and insulin resistance, as well as deteriorations in bone metabolism [1,2].

MetS is a well described but incompletely understood condition that presents a cluster of risk factors, including insulin resistance, abdominal obesity, dyslipidemia, and hypertension [4]. It may also underlie cardiovascular diseases and type 2 diabetes [5,6]. The metabolic alterations that occur during menopause seem to increase the likelihood of developing MetS [7,8]. Additionally, menopause is associated with a shift in fat distribution toward the abdomen and an increase in fat mass [9]. Yet it is still unclear if the aging process or hormonal fluctuations are to blame for these alterations. These hormonal changes not only influence metabolic and skeletal health but also contribute to the onset and progression of various menopausal symptoms, including vasomotor and urogenital complaints.

Recent studies have increasingly focused on the intricate relationships between menopause, MetS, and bone health. Estrogen deficiency plays a critical role in this complex relationship, contributing to endothelial dysfunction, increased adiposity, altered lipid metabolism, and reduced osteoblastic activity [10,11]. These hormonal changes may not only worsen the metabolic profile but also accelerate

bone resorption, thereby increasing the risk of osteoporosis and cardiovascular comorbidities [12,13]. Furthermore, the inflammatory environment associated with MetS, characterized by elevated cytokines such as tumor necrosis factor-α (TNF-α) and interleukin (IL)-6, may further aggravate both bone loss and menopausal symptom severity [12].

Despite growing evidence suggesting a relationship between menopausal symptoms, MetS, and bone mineral density (BMD) loss, the exact nature of these associations remains poorly defined. The research landscape presents a complex picture, with some investigations demonstrating clear associations between severe somatic symptoms and both MetS and low BMD [14–16], while other well-designed study has found no significant relationships [17]. This inconsistency in findings likely stems from the inherent complexity of menopause itself, as well as the diverse populations studied. Factors such as ethnic background, lifestyle patterns, nutritional habits, and individual genetic makeup may all influence how these conditions interact within different women. Moreover, it is still debated whether menopausal symptoms can serve as early clinical indicators of underlying metabolic or bone health problems.

Arising from these questions, we proposed the specific hypothesis that postmenopausal women exhibiting both low BMD and MetS would report greater severity of menopausal symptoms compared to those with either condition alone or neither. Recognizing the critical gaps in our understanding and the urgent clinical need to identify postmenopausal women at heightened risk for metabolic and bone health complications, we conducted this study to investigate the potential interrelationship among BMD, MetS, and menopause-related symptoms, aiming to enhance insight into the shared pathophysiological pathways and inform potential screening strategies in this population

2. Materials and Methods

2.1 Study Design and Ethics

This single center prospective cross-sectional study was carried out at the Obstetrics and Gynaecology Department of Liv Hospital Vadistanbul, Istanbul, Turkiye, with data collected from January 2023 to June 2023. The study was initiated after obtaining the approval of the ethics committee at Istanbul Istinye University (Decision date: 21 December 2022, decision no: 3/2022.K-95) and conducted in compliance with the relevant ethical guidelines and the Declaration of Helsinki. Written informed consent was obtained from all participants.

2.2 Study Population and Data Collection

The study included postmenopausal women aged between 45 and 65 years who had applied for annual checkup to our outpatient clinic during the study period. Women who had a follicle-stimulating hormone (FSH) level of $>$30 IU/L and had been amenorrheic for at least 12 consecutive months without an underlying medical condition, were defined to be postmenopausal [1]. The exclusion criteria were as follows: surgical menopause, premature menopause, being amenorrheic for more than 10 years, history of pelvic surgery, cancer, chemotherapy, radiotherapy, hormone replacement therapy, thyroid disease (including both hypo- and hyperthyroidism), Cushing's disease, diabetes mellitus, polycystic ovary syndrome, adrenal disorders, and the use of medications that affect bone metabolism (e.g., bisphosphonates, corticosteroids, selective estrogen receptor modulators) or thyroid function.

At the time of hospital admission, data on the demographic and anthropometric features, smoking and exercise status, pregnancy history and the laboratory and radiological findings were recorded in the patient files. All laboratory and clinical measurements followed standardized hospital protocols.

2.3 Anthropometric Measurements

Height and weight were measured in a standardized examination room at Liv Hospital Vadistanbul using a wall-mounted Harpenden stadiometer (Holtain Ltd, Crymych, UK) and calibrated Seca 767 digital scale (Seca GmbH, Hamburg, Germany). Body mass index (BMI) was calculated by dividing the weight (kg) by the square of the height (m^2). Waist and hip circumferences were measured in duplicate with a non-stretch tape measure at the midpoint between the iliac crest and lowest rib, and at the widest part of the buttocks, respectively, per World Health Organization (WHO) STEPwise approach to Surveillance (STEPS) protocol. Waist-to-hip ratio (WHR) was calculated by dividing the waist circumference by the hip circumference using the same units of measurement [18]. Systolic blood pressure and diastolic blood pressure were measured using an Omron M3 sphygmomanometer (HEM-7134-E, Omron Healthcare, Kyoto, Japan) after at least 15 minutes of rest.

2.4 Laboratory Analysis

Venous blood samples were collected from all participants after 12 hours of fasting to analyze biochemical parameters, including serum triglycerides (TG), high density lipoprotein cholesterol (HDL-C), fasting glucose, vitamin D, and vitamin B12 levels. All samples were analyzed in a single certified laboratory, using the same methodology.

2.5 Diagnosis of MetS

MetS diagnoses were clinically confirmed by the study's principal investigator (gynecologist) and an internal medicine specialist at Liv Hospital Vadistanbul, based on National Cholesterol Education Program-Adult Treatment Panel III (NCEP-ATP III) criteria. MetS was defined as the presence of at least three of the following NCEP-ATP III criteria: (i) Abdominal obesity, characterized by a waist circumference of $\geq$88 cm in women; (ii) Serum TG of $\geq$150 mg/dL, or receiving drug treatment for high TG; (iii) Serum HDL-C $<$50 mg/dL, or receiving drug treatment for low

HDL-C; (iv) Fasting plasma glucose levels of ≥100 mg/dL, or receiving drug treatment for elevated blood glucose; (v) Blood pressure levels of ≥130/85 mmHg, or receiving drug treatment for elevated blood pressure [19]. The MetS and non-MetS groups were created in accordance with these criteria.

2.6 BMD Measurement

The BMD was assessed in the hospital's dedicated dual-energy X-ray absorptiometry (DXA) suite by two certified radiologic technologists using a GE Lunar DPX Pro Densitometer Machine (GE Medical Systems, Waukesha, WI, USA), calibrated daily. Participants were positioned supine for lumbar spine (L1–L4) and lateral decubitus for femoral neck scans per manufacturer protocols. The DXA scans were obtained following the standard protocol recommended by the manufacturer for scanning and analysis. Daily quality control procedures were conducted to ensure reliable results. BMD measurements were performed from two locations: the lumbar spine (anteroposterior projection at L1–L4) and the femoral neck. The women were categorized based on the lowest T-score obtained from either the L1–L4 lumbar spine or the femur neck. The classification system of the WHO was used to define normal BMD (–1 ≤T-score), osteopenia (–2.5 < T-score < –1), and osteoporosis (T-score ≤–2.5) [20]. Women with osteopenia or osteoporosis were pooled into the low BMD group.

2.7 Menopausal Symptoms

To assess menopausal symptoms, the Menopause Rating Scale (MRS) questionnaire was employed [21,22]. The MRS questionnaire was administered face-to-face by trained research nurses in a private clinic room. The MRS consists of 11 items that are grouped into three symptom categories: somatic, psychological, and urogenital symptoms. Each symptom is rated on a scale from 0 (no symptoms) to 4 (very severe symptoms). The total score is a measure of the overall impact of menopause on quality of life. The somatic subcategory includes hot flashes, heart discomfort, sleeping problems, and muscle and joint issues (items 1–3 and 11). The psychological subcategory includes depressive mood, irritability, anxiety, and physical and mental exhaustion (items 4–7). The urogenital subcategory includes sexual problems, bladder problems and vaginal dryness (items 8–10). The scores for each symptom are summed to obtain the total MRS score. A higher total score indicates greater severity of menopausal symptoms.

2.8 Sample Size Calculation

Power analysis was performed using the G*Power software (version 3.1.9; Heinrich Heine University Düsseldorf, Düsseldorf, Germany). We targeted a power of 80% with the classical significance level of 5% ($p = 0.05$). According to the effect size (d = 0.518) obtained from the study by Cengiz *et al.* [14], a total sample size of at least 120 patients (60 patients for each group) was deemed necessary to perform the study with sufficient power. The formula we use in that analysis is $n = 2\,(Z_{1-\alpha/2} + Z_{1-\beta})^2/d^2$. Where n represents the sample size per group, $Z_{1-\alpha/2}$ is the Z-score corresponding to the two-tailed significance level (for $\alpha = 0.05$, $Z_{0.975} = 1.96$), $Z_{1-\beta}$ is the Z-score corresponding to the desired power (for 80% power, $Z_{0.80} = 0.84$), and d is Cohen's d effect size (obtained as 0.518 from Cengiz *et al.* [14]).

2.9 Statistical Analysis

All data obtained from records or measurements performed for the study were transferred to an SPSS database (SPSS for Windows, v25.0; IBM Corp. Armonk, NY, USA) and all analyses were performed with the same software. For descriptive data, we used frequency (percentage) for categorical variables and performed comparisons with chi-square tests. Numerical data were presented based on normality of distribution [checked with histograms and quantile-quantile (Q-Q) plots]. Normally distributed variables were summarized using mean ± standard deviation, while median (25th percentile–75th percentile) was used for those not fulfilling normal distribution. The Student's *t*-test was used to analyze normally distributed numerical data and the Mann-Whitney U test was used to analyze non-normally distributed numerical data. Pearson or Spearman (or point biserial correlation) coefficients were calculated to evaluate directional relationships between MRS scores and other relevant variables. Two-way analysis of variance (ANOVA) was used to evaluate potential interactions between MetS and BMD in terms of MRS scores. Multivariable linear regression analysis was used to determine significant factors independently associated with MRS scores. Statistically significant variables according to univariate analysis results were included to regression analysis. *p* values less than 0.05 were considered statistically significant.

3. Results

During the study period, 326 postmenopausal women were examined for eligibility and 193 women who met the inclusion criteria were analyzed.

3.1 Participant Characteristics and MetS Associations

The mean age of all participants was 51.88 ± 4.99 years. Women with MetS were significantly older and had been in menopause for a longer period than those without MetS ($p = 0.001$ for both). The BMI and WHR of women with MetS were significantly higher than those without MetS ($p < 0.001$). The percentage of women exercising regularly was significantly higher in the non-MetS group ($p = 0.001$). There was no significant difference in terms of BMD values and MRS (total and sub-scores) between women with and without MetS (Table 1).

Table 1. Participant characteristics, laboratory measurements and Menopause Rating Scale (MRS) scale scores with regard to metabolic syndrome (MetS).

	Overall	MetS		*p*
		No (n = 117)	Yes (n = 76)	
Age, years	51.88 ± 4.99	50.91 ± 4.51	53.37 ± 5.33	**0.001**†
Body mass index (BMI), kg/m^2	26.17 (22.64–31.22)	24.84 (22.23–28.24)	30.84 (25.32–33.30)	**<0.001**‡
Waist-to-hip ratio (WHR)	0.81 (0.75–0.88)	0.79 (0.75–0.85)	0.84 (0.78–0.90)	**<0.001**‡
Parous (>1 pregnancy >20 weeks)	168 (87.05%)	94 (80.34%)	74 (97.37%)	**0.001**§
Education status				
Primary school	125 (64.77%)	84 (71.79%)	41 (53.95%)	
High school	48 (24.87%)	26 (22.22%)	22 (28.95%)	**0.014**§
University	20 (10.36%)	7 (5.98%)	13 (17.11%)	
Smoking	44 (22.80%)	28 (23.93%)	16 (21.05%)	0.772§
Exercise regularly	55 (28.50%)	44 (37.61%)	11 (14.47%)	**0.001**§
Bone mineral density (BMD)				
Normal	96 (49.74%)	60 (51.28%)	36 (47.37%)	0.595§
Low	97 (50.26%)	57 (48.72%)	40 (52.63%)	
Vitamin D, ng/mL	32.5 (25.0–41.2)	32.8 (25.7–41.4)	32.3 (22.7–40.8)	0.094‡
Vitamin B12, ng/mL	419 (328.00–558.00)	419 (331.00–567.00)	400 (318.45–527.00)	0.301‡
Years since menopause	2 (1.0–5.0)	2 (1.0–4.0)	4 (1.0–6.5)	**0.001**‡
MRS score				
Total	17.09 ± 7.18	17.27 ± 7.53	16.80 ± 6.66	0.658†
Somatic	6.15 ± 3.21	6.43 ± 3.36	5.72 ± 2.95	0.138†
Psychological	6.78 ± 3.60	6.74 ± 3.64	6.83 ± 3.55	0.872†
Urogenital	4 (2.0–6.0)	4 (2.0–6.0)	4 (1.5–7.0)	0.704‡

Descriptive statistics were presented using mean ± standard deviation for normally distributed continuous variables, median (25th percentile–75th percentile) for non-normally distributed continuous variables and frequency (percentage) for categorical variables.

† Student's *t*-test, ‡ Mann-Whitney U test, § Chi-square test. Statistically significant *p* values are shown in bold.

3.2 BMD Groups and Associated Factors

With respect to BMD groups, women with low BMD were significantly older ($p = 0.012$), had been in menopause for longer ($p = 0.006$), and had lower BMI ($p = 0.016$). Notably, women with normal BMD had lower frequency of exercising regularly ($p = 0.012$) and lower vitamin B12 concentrations ($p = 0.015$). In terms of MRS scores, the only subcategory with significant difference was the urogenital symptom score, which was significantly higher (worse) in women with low BMD ($p = 0.019$) (Table 2).

3.3 Correlational Analyses Between MRS Scores and Clinical Variables

With respect to directional relationships between symptoms and other factors, we detected that age had significant but weak negative correlations with MRS total score (r = –0.184, $p = 0.011$), somatic symptom score (r = –0.291, $p < 0.001$), and psychological symptom score (r = –0.187, $p = 0.009$). MRS somatic symptom score and BMI also showed a weak negative correlation (r = –0.145, $p = 0.044$) (Table 3).

3.4 Interaction Effects of MetS and BMD on Menopausal Symptoms

According to two-way ANOVA results, we found no interaction between MetS and BMD in terms of MRS scores. In addition, all between group analysis results were non-significant except MRS urogenital symptom score for BMD groups ($p = 0.023$), in line with univariate analysis results (Table 4).

3.5 Independent Predictors of Menopausal Symptoms

According to multivariable linear regression analysis results, high age was independently associated with low MRS Total score (b: –0.264, 95% CI: –0.467 to –0.062, $p = 0.011$), low MRS Somatic score (b: –0.181, 95% CI: –0.269 to –0.093, $p < 0.001$) and low MRS Psychological score (b: –0.135, 95% CI: –0.236 to –0.034, $p = 0.009$). Also, low BMD was independently associated with MRS urogenital score (b: 0.776, 95% CI: 0.006 to 1.545, $p = 0.048$) (Table 5).

4. Discussion

The current study was designed to assess menopausal symptoms, MetS and BMD findings in our postmenopausal cohort and to identify possible relationships between the

Table 2. Comparison of normal and low BMD groups in terms of characteristics, laboratory measurements and MRS scale scores.

	BMD		*p*
	Normal (n = 96)	Low (n = 97)	
Age, years	50.97 ± 4.74	52.77 ± 5.09	**0.012**†
BMI, kg/m^2	28.19 (23.75–31.22)	25.32 (21.67–31.25)	**0.016**‡
WHR	0.81 (0.76–0.90)	0.80 (0.75–0.87)	0.171‡
Parous (>1 pregnancy >20 weeks)	88 (91.67%)	80 (82.47%)	0.092§
Education status			
Primary school	53 (55.21%)	72 (74.23%)	
High school	29 (30.21%)	19 (19.59%)	**0.017**§
University	14 (14.58%)	6 (6.19%)	
Smoking	18 (18.75%)	26 (26.80%)	0.245§
Exercise regularly	19 (19.79%)	36 (37.11%)	**0.012**§
MetS	36 (37.50%)	40 (41.24%)	0.595§
Vitamin D, ng/mL	32.80 (26.35–41.10)	32.00 (24.20–41.40)	0.415‡
Vitamin B12, ng/mL	368.5 (298.0–468.6)	432.0 (332.0–595.0)	**0.015**‡
Years since menopause	2 (1–3)	4 (1–6)	**0.006**‡
MRS score			
Total	16.48 ± 6.64	17.69 ± 7.68	0.242†
Somatic	5.91 ± 3.16	6.39 ± 3.26	0.295†
Psychological	6.80 ± 3.56	6.75 ± 3.64	0.924†
Urogenital	3 (1–6)	5 (3–6)	**0.019**‡

Descriptive statistics were presented using mean ± standard deviation for normally distributed continuous variables, median (25th percentile–75th percentile) for non-normally distributed continuous variables and frequency (percentage) for categorical variables.

† Student's *t*-test, ‡ Mann-Whitney U test, § Chi-square test. Statistically significant *p* values are shown in bold.

Table 3. Correlations between MRS scores and other variables.

		Total	Somatic	Psychological	Urogenital
Age, years	R	–0.184†	–0.291†	–0.187†	0.093‡
	P	**0.011**	**<0.001**	**0.009**	0.197
BMI, kg/m^2	R	–0.030‡	–0.145‡	0.090‡	–0.102‡
	P	0.679	**0.044**	0.215	0.158
WHR	R	0.058‡	–0.107‡	0.099‡	0.063‡
	P	0.425	0.139	0.169	0.386
Parous (>1 pregnancy >20 weeks)	R	0.041§	–0.011§	0.023§	0.082‡
	P	0.568	0.881	0.747	0.256
Education status	R	–0.063‡	–0.140‡	–0.045‡	0.077‡
	P	0.384	0.053	0.530	0.284
Smoking	R	0.079§	0.055§	0.092§	0.042‡
	P	0.272	0.444	0.202	0.558
Exercise regularly	R	0.052§	0.081§	0.033§	0.027‡
	P	0.477	0.260	0.650	0.712
Vitamin D, ng/mL	R	–0.029‡	–0.053‡	–0.093‡	0.093‡
	P	0.692	0.466	0.199	0.197
Vitamin B12, ng/mL	R	0.029‡	0.017‡	0.076‡	0.014‡
	P	0.689	0.817	0.294	0.852
Years since menopause	R	–0.071‡	–0.136‡	–0.042‡	0.058‡
	P	0.325	0.059	0.563	0.427

† Pearson correlation coefficient, ‡ Spearman correlation coefficient, § Point biserial correlation coefficient. Statistically significant *p* values are shown in bold.

Table 4. MRS scores with regard to MetS and BMD, two-way analysis of variance (ANOVA) results.

		MetS		p (MetS)†	p (BMD)‡	p (MetS BMD)§
		No (n = 117)	Yes (n = 76)			
MRS total score						
BMD	Normal (n = 96)	16.63 ± 7.51	16.22 ± 4.94	0.628	0.257	0.921
	Low (n = 97)	17.95 ± 7.56	17.33 ± 7.92			
MRS somatic score						
BMD	Normal (n = 96)	6.12 ± 3.32	5.56 ± 2.87	0.130	0.313	0.737
	Low (n = 97)	6.75 ± 3.39	5.88 ± 3.05			
MRS psychological score						
BMD	Normal (n = 96)	6.53 ± 3.73	7.25 ± 3.26	0.850	0.730	0.249
	Low (n = 97)	6.96 ± 3.56	6.45 ± 3.78			
MRS urogenital score						
BMD	Normal (n = 96)	3.98 ± 2.95	3.42 ± 2.81	0.797	0.023	0.095
	Low (n = 97)	4.23 ± 2.13	5.00 ± 2.94			

Descriptive statistics were presented using mean ± standard deviation.

† Between groups analysis for MetS, ‡ Between groups analysis for BMD, § Interaction between MetS and BMD.

Table 5. Significant factors independently associated with MRS scores, multivariable linear regression analysis.

	Unstandardized β	Standard error	Standardized β	p	95% Confidence interval for β
MRS total score, $R^2 = 0.034$, $F = 6.661$, $p = 0.011$					
(Constant)	30.808	5.340		<0.001	20.274, 41.342
Age, years	–0.264	0.102	–0.184	**0.011**	–0.467, –0.062
MRS somatic score, $R^2 = 0.099$, $F = 10.401$, $p < 0.001$					
(Constant)	17.458	2.489		<0.001	12.548, 22.368
Age, years	–0.181	0.045	–0.281	**<0.001**	–0.269, –0.093
BMI, kg/m^2	–0.071	0.042	–0.118	0.090	–0.153, 0.011
MRS psychological score, $R^2 = 0.035$, $F = 6.936$, $p = 0.009$					
(Constant)	13.777	2.670		<0.001	8.510, 19.044
Age, years	–0.135	0.051	–0.187	**0.009**	–0.236, –0.034
MRS urogenital score, $R^2 = 0.020$, $F = 3.956$, $p = 0.048$					
(Constant)	3.771	0.276		<0.001	3.226, 4.316
Low BMD	0.776	0.390	0.142	**0.048**	0.006, 1.545

Statistically significant p values are shown in bold.

severity of menopausal symptoms and MetS and/or low BMD. Our study revealed that approximately 40% of our patients had MetS, 50% had low BMD, and 21% had co-existence of MetS and low BMD. Despite the expected links between MetS and menopausal symptoms due to metabolic dysregulation, our findings did not confirm this relationship. The presence of only MetS was not associated with increased total, somatic, psychological, or urogenital MRS scores in postmenopausal women. However, the presence of low BMD and the co-existence of low BMD and MetS were found to be associated with worse urogenital symptoms.

MetS is a complex condition that emerges in relation with many underlying properties and causes risks for cardiovascular disease and diabetes, often manifesting as insulin resistance, high blood pressure, elevated triglyceride levels, low levels of high-density lipoprotein cholesterol, and obesity (especially central obesity) [4]. The reported prevalence of MetS varies, with estimates ranging from 20% to 55% among postmenopausal women. In the current study, we found the frequency of MetS in naturally menopausal women to be approximately 40%, which aligns with previously reported rates in this population. Our results indicated a positive association between MetS and high pregnancy rates and the time elapsed since menopause onset, while regular exercise appeared to be protective against MetS. Notably, we did not find a significant correlation between MetS and menopause symptom severity, which contradicts several previous reports.

A previous study has suggested a decline in quality of life in postmenopausal women with MetS [15]. While estrogen deficiency is linked to MetS [10,11]. The inconsistent effects of Hormone Replacement Therapy (HRT) suggest other factors may be involved [23–25]. Furthermore, the role of exercise in metabolic regulation has been widely documented, and the findings of the recent studies

reinforce its protective effects against MetS [26]. Nevertheless, our study did not observe significant associations between MetS and menopause symptom scores. One study has demonstrated increased MRS scores, particularly somatic and vasomotor symptoms, in patients with MetS [26]. Others have identified significant positive correlations between abdominal obesity, TG, blood pressure, and MRS scores [15]. While many studies support a link between MetS and menopausal symptoms [16,27], there is a conflicting study that reports no significant relationship [17], which may suggest that lifestyle, genetic predisposition or aging alone may influence this association. Although hormonal changes and lipid alterations have been proposed as potential mechanisms linking MetS and menopause, the cross-sectional nature of our study limits our ability to infer causality.

Another significant health challenge faced by postmenopausal women is osteoporosis. Menopausal symptoms, particularly vasomotor and urogenital complaints, tend to fluctuate over time. A meta-analysis including 35,445 women reported that hot flashes typically persist for around 4 years, peaking around 1 year prior to the final menstrual period and gradually decreasing thereafter [28]. In contrast, vulvovaginal symptoms often increase postmenopause, reaching a plateau prevalence of over 84% by the sixth year [29]. Estrogen loss is a key driver of these symptoms and is also known to increase osteoclastic activity while reducing osteoblastic function, thereby contributing to bone loss [12,13]. The pathophysiological connection between menopausal symptoms and BMD can be explained through several mechanisms, including decline in estrogen, increased inflammation and oxidation, changes in calcium and vitamin D levels, co-existence of hormonal dysregulation and the aging processes, which can come together to create a general deceleration in the renewal of bone tissue [12,13]. In the present study, patients with low BMD were older, had been in menopause for longer, and had lower BMI. Our findings align with previously established risk factors for osteoporosis. Interestingly, a higher proportion of women in the low BMD group engaged in regular exercise, which may reflect a proactive approach to osteoporosis prevention rather than a causal relationship. Women with low BMD exhibited higher MRS urogenital scores, but other symptom scores remained unaffected. Those with co-existing low BMD and MetS were older, had been menopausal longer, and also reported higher MRS urogenital scores. Previous studies investigating the relationship between menopausal symptoms, BMD, and MetS have yielded conflicting results. While some found associations between severe somatic symptoms and both MetS and low BMD [15,16], others reported fewer vasomotor symptoms in women with MetS [15]. Vaginal dryness has also been linked to greater bone loss in certain studies [30,31]. Prior research has linked decreased BMD with severe vasomotor symptoms such as hot flashes and night sweats [32–34]. However, our study did not observe a direct relationship between vasomotor symptoms and BMD. Instead, we identified a significant association between BMD loss and urogenital symptoms. This matches the findings from the AGATA study, which reported genitourinary syndrome in 79.1% of women and an increasing prevalence over time after menopause [35]. These findings suggest that postmenopausal urogenital symptoms could serve as an early indicator of declining BMD, warranting further investigation into potential shared pathophysiological pathways.

The current study demonstrated a correlation between severe urogenital symptoms in postmenopausal women and a decline in BMD. If confirmed in future studies, this association could contribute to improved screening strategies. Severe urogenital symptoms can be used as an indicator to identify women at risk of low BMD and osteoporosis. Taking measures to protect bone health and implementing pharmacological interventions, when necessary, may be vital for preventing fractures in this particular patient group.

Due to the single-center design and the potential adverse impacts of analyzing a homogenous population, our findings may not be generalizable to broader postmenopausal populations. The cross-sectional design of the study may limit the possibility to establish long-term causal links between BMD and MetS in postmenopausal women. Since the primary aim of the study was to investigate the effects of MetS and low BMD on postmenopausal symptoms, only postmenopausal women were included. However, excluding premenopausal women compromises the evaluation of the impact of non-menopausal factors on MetS and BMD. Additionally, selection bias may be present, as our cohort consisted of women presenting for routine checkups, potentially representing a health-conscious population. Although the MRS urogenital subscale provided a standardized measure, future studies might benefit from supplementing it with condition-specific tools (e.g., Female Sexual Function Index for sexual health) to capture nuanced symptom profiles. Furthermore, the subgroup with both MetS and low BMD included only 40 individuals, which may be considered small. Although expanding this group would improve statistical power, strict inclusion and exclusion criteria were necessary to minimize confounding effects, especially in older women with multiple comorbidities. This limited the number of eligible participants. Future prospective, long-term cohort studies with broader recruitment criteria may help to better clarify these associations.

5. Conclusions

The present study demonstrated that while MetS did not correlate with menopausal symptom severity, low BMD was significantly associated with worse urogenital symptoms. This relationship remained significant in women with both low BMD and MetS, suggesting that urogenital symptoms may be a potential marker of osteoporosis risk in postmenopausal women. Although the observational de-

sign limits causal interpretations, our findings emphasize the need for further large-scale investigations into the relationship between BMD loss and urogenital symptoms.

Abbreviations

BMD, bone mineral density; MetS, metabolic syndrome; BMI, body mass index; FSH, follicle-stimulating hormone; WHO, World Health Organization; STEPS, STEPwise approach to Surveillance; WHR, waist-to-hip ratio; TG, triglycerides; HDL-C, high density lipoprotein cholesterol; MRS, Menopause Rating Scale; HRT, Hormone Replacement Therapy; NCEP-ATP III, National Cholesterol Education Program-Adult Treatment Panel III; TNF-α, tumor necrosis factor-α; IL, interleukin; DXA, dual-energy X-ray absorptiometry; ANOVA, analysis of variance; Q-Q, quantile-quantile.

Availability of Data and Materials

The datasets generated and analyzed during the current study are available from the corresponding author upon reasonable request.

Author Contributions

AAM and SC designed the study. AAM and SC analyzed the data and performed the statistical analysis. AAM collected data. SC interpreted of data of the work. Both authors contributed to editorial changes in the manuscript. Both authors read and approved the final manuscript. Both authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

The study was initiated after obtaining the approval of the ethics committee at Istanbul Istinye University (Decision date: 21 December 2022, decision no: 3/2022.K-95) and conducted in compliance with the relevant ethical guidelines and the Declaration of Helsinki. Written informed consent was obtained from all participants.

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Conflict of Interest

The authors declare no conflict of interest.

Declaration of AI and AI-Assisted Technologies in the Writing Process

During the preparation of this work, the authors used ChatGPT to check spelling and grammar. After using this tool, the authors reviewed and edited the content as needed and take full responsibility for the content of the publication.

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