Clinical Research Report

Journal of INTERNATIONAL MEDICAL RESEARCH

Relationship between vasomotor symptoms and metabolic syndrome in postmenopausal women

Journal of International Medical Research
2018, Vol. 46(10) 4157–4166

DOI: 10.1177/0300060518790709
journals.sagepub.com/home/imr
SAGE

Sena Sayan[1], Tanju Pekin[2] and Begüm Yıldızhan[2]

Abstract

Objective: This study was performed to compare the vasomotor symptoms and bone mineral density of postmenopausal women with and without metabolic syndrome.

Methods: We performed a cross-sectional study of 200 postmenopausal women attending routine health check-ups at Marmara Faculty of Medicine Pendik Training and Research Hospital from June 2015 to December 2015. The vasomotor symptoms scored were hot flashes and night sweats. Metabolic syndrome was defined using the consensus criteria of the International Diabetes Federation and the American Heart Association/National Heart, Lung, and Blood Institute.

Results: Women with vasomotor symptoms had no metabolic syndrome and were younger than those without vasomotor symptoms. There was no significant difference in vasomotor symptoms between patients with osteopenia in the femoral neck, total femur, and spine and patients with normal bone mineral density. The vasomotor symptoms were similar between smokers and nonsmokers.

Conclusion: The presence of metabolic symptoms is inversely associated with metabolic syndrome in postmenopausal women. Lipid abnormalities and a high body mass index may be important metabolic components associated with these symptoms. No relationship is present between vasomotor symptoms and the bone mineral density of the spine, femoral neck, and total femur.

Keywords

Menopause, vasomotor symptoms, metabolic syndrome, bone mineral density, hot flashes, night sweats

Date received: 22 March 2018; accepted: 3 July 2018

[1]Ministry of Health of the Republic of Turkey, University of Health Sciences, Van Training and Research Hospital, Obstetrics and Gynecology Clinic, Van, Turkey
[2]Marmara University, Department of Obstetrics and Gynecology, Medical Faculty, Istanbul, Turkey

Corresponding author:
Sena Sayan, Specialist Doctor, Ministry of Health of the Republic of Turkey, University of Health Sciences, Van Training and Research Hospital, Obstetrics and Gynecology Clinic, Van 65100, Turkey.
Email: senasay@hotmail.com

Introduction

Menopause is defined as the lack of menstruation for at least 1 year. The increase in life expectancy has not changed the average age of menopause.[1] Ovarian dysfunction and decreased estrogen levels occur during menopause and cause symptoms such as hot flashes, night sweats, mood changes, and sleep disorders, all of which affect women's quality of life. In addition, the long-term lack of estrogen may lead to life-threatening conditions including cardiovascular disease and osteoporosis. Approximately 60% to 80% of postmenopausal women report that vasomotor symptoms cause discomfort and negatively influence their quality of life.[2] The blood lipid levels are substantially different between premenopausal and postmenopausal women. Compared with premenopausal women, the total cholesterol, low-density lipoprotein (LDL), and triglyceride levels are higher and the high-density lipoprotein level is lower in postmenopausal women. These changes are associated with an increased risk of cardiovascular disease.[3]

Metabolic syndrome (MetS) is an endocrinopathy with a risk of mortality. MetS begins with insulin resistance and proceeds to interlaced systemic disorders such as abdominal obesity, glucose intolerance, diabetes mellitus, dyslipidemia, hypertension, and coronary artery disease.[4] Different definitions of MetS have been proposed, but in 2009, a consensus regarding diagnosis was established. These consensus criteria were used to diagnose MetS in the present study (Table 1). The prevalence of MetS in Turkey is very high, affecting 28% of men and 40% of women.[5]

The role of hormone replacement therapy in the prevention of vasomotor symptoms is considerably narrow, and no effective treatment is available to relieve the symptoms. Thus, identifying the causes that exacerbate the symptoms may allow for the development of new treatment options. In the present study, we compared the vasomotor symptoms and bone mineral density (BMD) of postmenopausal women with and without MetS.

Table 1. Consensus criteria (IDF + AHA/NHLBI) 2009[6].

Three of the following are necessary for a diagnosis of metabolic syndrome
Increased waist circumference of >88 cm (female)
Triglyceride level of ≥150 mg/dL
High-density lipoprotein cholesterol level of <40 mg/dL (male) or <50 mg/dL (female)
Blood pressure of ≥130/85 mmHg
Fasting blood glucose level of ≥100 mg/dL

IDF, International Diabetes Federation; AHA/NHLBI, American Heart Association/National Heart, Lung, and Blood Institute.

Materials and methods

We performed a cross-sectional study of postmenopausal women who were attending routine health check-ups at Marmara University Faculty of Medicine Pendik Training and Research Hospital Department of Obstetrics and Gynecology from June 2015 to December 2015. The Marmara University School of Medicine Ethics Committee approved the study protocol. The participants were divided into two groups: postmenopausal patients with MetS and healthy postmenopausal women (the control group).

Patients

The demographic and metabolic characteristics, vasomotor symptoms, and BMD of the two groups were compared. This study was prospectively conducted and planned as a case-control study. The case and control groups included patients who had been referred to the menopause outpatient clinic of our hospital, had not had menstruation for at least 1 year, and had a blood

follicle-stimulating hormone level of >40 IU/L. The 2009 Consensus Criteria established according to the criteria of International Diabetes Federation (IDF) and American Heart Association/National Heart, Lung, and Blood Institute (AHA/NHLBI) were used to diagnose MetS. While we assessed the patients' vasomotor symptoms, we questioned the patients about the presence of hot flashes and night sweats. If such symptoms were present, the patients rated their effect on quality of life using a scale ranging from 1 to 10. The results were grouped as mild (1–5 points), moderate (5–7 points), and severe (7–10 points). All participating women were informed in detail about the work done in the study. All were given written patient information forms, and upon reading and agreeing to join the study, the patients signed informed consent forms.

Patients who had been menopausal for at least 10 years were not included in the study because of a decline in vasomotor symptoms after 10 years.[6] Patients with surgery-induced menopause were also excluded. Whether the patients had MetS was unknown before the study began. The diagnosis of MetS was made according to the 2009 Consensus Criteria (IDF and AHA/NHLBI).[7]

Patients shown to have hypothyroidism or hyperthyroidism by thyroid function tests were not included in the study. Patients with malignancy or suspected malignancy and patients who took mood stabilizers were also excluded.

Data collection

All patients' age; number of pregnancies; smoking habit; alcohol use; ages at menopause and menarche; occurrence of hot flashes and night sweating; obstetric, gynecological, medical, and surgical histories; and family history were obtained to derive a detailed medical history. The height and weight of all women participating in the study were measured, and their body mass indexes (BMIs) were calculated accordingly. All participants underwent a detailed physical examination including speculum examination, cervical smear, pelvic examination, and transvaginal ultrasonography followed by bilateral mammography. Blood pressure measurements were performed with an Omron M2 digital fully automatic blood pressure monitor (Omron Healthcare, Kyoto, Japan); the measurements were obtained from the brachial artery by fitting a cuff to the right arm with the patient in a rested state in a sitting position in our outpatient clinic. All data were noted in the patient evaluation form. Venous blood samples were taken from all participants between 08:00 and 10:00 after 8 to 10 hours of fasting to determine the fasting blood glucose, blood urea nitrogen, blood creatinine, aspartate transaminase, alanine transaminase, hemogram, LDL, HDL, triglyceride, total cholesterol, and thyroid-stimulating hormone levels. All samples were spectrophotometrically examined using an Accu-Chek device (D-68298; Roche Diagnostics GmbH, Mannheim, Germany). For the diagnosis of osteoporosis, BMD was measured using the same X-ray absorptiometry instrument (Lunar DPX-L; Lunar Corporation, Madison, WI, USA). Lumbar vertebral scans were performed in the supine position. According to the World Health Organization classification, bone density was determined using the T score (a score of -1 to -2.5 indicates osteopenia, and a score of -2.5 or less indicates osteoporosis).

Statistical analysis

Mean, median, standard deviation, minimum, maximum, ratio, and frequency values were used for descriptive statistics of the data. The distribution of the variables was checked using the Kolmogorov–Smirnov test. Analysis of quantitative data

was performed with the Mann–Whitney U test and independent-samples t-test. Pearson and Spearman correlation analyses were used for the correlation analysis. Effect-level logistic regression analysis was performed using SSPS 21.0 software (IBM Corp., Armonk, NY, USA). The significance level was $p < 0.05$.

Results

Two hundred postmenopausal women were included in this study. The characteristics of the study group are shown in Table 2 (categorical data) and Table 3 (measurement data). The laboratory characteristics of the study group are shown in Table 4.

No significant difference in vasomotor symptoms was found between smokers and nonsmokers. In the study group, 2 patients without vasomotor symptoms were smokers whereas 36 were nonsmokers. No significant difference was found between the two groups. Three patients with moderate vasomotor symptoms were smokers and 14 were nonsmokers. Of the patients with severe vasomotor symptoms, 14 were smokers and 131 were nonsmokers (Table 5).

MetS was correlated with vasomotor symptoms. In the study group, 14 patients without vasomotor symptoms had MetS, whereas 24 patients did not. The difference between the two groups was statistically significant ($p = 0.037$). Among patients with moderate vasomotor symptoms, 1 had MetS and 16 did not. The difference

Table 2. Characteristics of the study group (categorical data).

Variable	Category	f (frequency)	%
Number of children	0	18	5.2
	1	11	5.7
	2	75	39.1
	3	57	29.7
	4	31	16.1
	≥5	8	4.2
	Total	192	100
Smoking status	Yes	19	9.5
	No	181	90.5
	Total	200	100
Metabolic syndrome	Present	48	24.0
	Absent	152	76.0
	Total	200	100
Vasomotor symptoms	Severe	145	72.5
	Moderate	17	8.5
	None	38	19.0
	Total	200	100

Table 3. Characteristics of the study group (measurement data).

Variable	
Age (years)	51.9 ± 5.65
BMI (kg/ cm^2)	30.05 ± 4.32
Menopause age (years)	46.8 ± 5.2
Menarche age (years)	12.8 ± 1.1
Height (cm)	160.1 ± 5.6
Weight (kg)	76.9 ± 10.5
SBP (mmHg)	123.4 ± 9.6
DBP (mmHg)	80.2 ± 6.7

The data are presented as mean ± standard deviation. BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure.

Table 4. Laboratory characteristics of the study group (measurement data).

Variable	
LDL cholesterol (mg/dL)	141.6 ± 32.3
HDL cholesterol (mg/dL)	58.1 ± 10.7
Total cholesterol (mg/dL)	232.4 ± 38.3
Glucose (mg/dL)	95.7 ± 16.1
Hemoglobin (mg/dL)	13.1 ± 5.6
Spinal BMD	−0.42 ± 1.8
Femoral neck BMD	−0.20 ± 1.0
Total femoral BMD	−0.40 ± 1.2

The data are presented as mean ± standard deviation. LDL, low-density lipoprotein; HDL, high-density lipoprotein; BMD, bone mineral density.

Table 5. Comparison of vasomotor symptoms of smokers and nonsmokers.

		Nonsmokers	Smokers	p value
Severity of vasomotor symptoms	None	36 (19.9)	2 (10.5)	0.348
	Moderate	14 (7.7)	3 (15.8)	0.366
	Severe	131 (72.4)	14 (73.7)	0.578

The data are presented as n (%).

Table 6. Comparison of vasomotor symptoms of patients with and without MetS.

		With MetS	Without MetS	p value
Severity of vasomotor symptoms	None	14 (29.2)	24 (15.8)	0.037
	Moderate	1 (2.1)	16 (10.5)	0.026
	Severe	33 (68.8)	112 (73.7)	0.164

The data are presented as n (%).
MetS, metabolic syndrome.

Table 7. Comparison of vasomotor symptoms of patients with and without osteopenic spinal BMD.

		Osteopenic spinal BMD	Normal spinal BMD	p value
Severity of vasomotor symptoms	None	16 (20.5)	22 (18.0)	0.382
	Moderate	4 (5.1)	13 (10.7)	0.359
	Severe	58 (74.4)	87(71.3)	0.961

The data are presented as n (%).
BMD, bone mineral density.

between the two groups was significant ($p = 0.026$). Of the patients with severe vasomotor symptoms, 33 had MetS and 112 did not (Table 6).

In the study group, spine BMD was not correlated with vasomotor symptoms. Sixteen of the patients with no vasomotor symptoms were osteopenic, whereas the spine BMD of the remaining 22 patients was normal; the difference was not significant. Among the patients with moderate vasomotor symptoms, the spine BMD measurements of 4 patients showed osteopenia, whereas 13 patients had normal results. The spine BMD measurements of 58 patients with severe vasomotor symptoms revealed osteopenia, whereas 87 had normal spinal BMD results (Table 7).

The mean spinal BMD T score was -0.36 in patients with MetS and -0.44 in patients without MetS ($p = 0.033$). The mean femoral neck BMD T score was -0.08 in patients with MetS and -0.24 in patients without MetS ($p = 0.002$). The mean total femoral BMD T score was -0.09 in patients with MetS and -0.08 in patients without MetS.

In the study group, the femoral neck BMD was not significantly correlated with vasomotor symptoms. Nine patients with vasomotor symptoms had osteopenia as indicated by their femoral neck BMD measurements, whereas 29 were normal.

Table 8. Comparison of vasomotor symptoms of patients with and without osteopenic femoral neck BMD.

		Osteopenic femoral neck BMD	Normal femoral neck BMD	p value
Severity of vasomotor symptoms	None	9 (16.7)	29 (19.9)	0.804
	Moderate	4 (7.4)	13 (8.9)	0.801
	Severe	41 (75.8)	104 (71.2)	0.533

The data are presented as n (%).
BMD, bone mineral density.

Table 9. Comparison of vasomotor symptoms of patients with and without osteopenic total femoral BMD.

		Osteopenic total femoral BMD	Normal total femoral BMD	p value
Severity of vasomotor symptoms	None	12 (21.8)	26 (17.9)	0.791
	Moderate	5 (9.1)	12 (8.3)	0.794
	Severe	38 (69.1)	107 (73.8)	0.495

The data are presented as n (%).
BMD, bone mineral density.

The femoral neck BMD measurements of 4 patients with moderate vasomotor symptoms revealed osteopenia, whereas those of 13 patients were normal. The femoral neck BMD measurements of 41 patients with severe vasomotor symptoms revealed osteopenia, whereas those of 104 patients were normal (Table 8).

In the study group, the total femoral BMD was not correlated with vasomotor symptoms. Twelve patients with vasomotor symptoms had osteopenia, whereas 26 were normal. The total femoral BMD measurements of 5 patients with moderate vasomotor symptoms revealed osteopenia, while those of 12 patients were normal. The total femoral BMD measurements of 38 patients with severe vasomotor symptoms revealed osteopenia, while those of 107 patients were normal (Table 9).

Discussion

Several studies in the literature have investigated the relationship between MetS and BMD during menopause. Jouyandeh et al.[8] found a 30.1% MetS prevalence using the ATPIII criteria. Furthermore, high abdominal obesity and hypertension were the most prevalent components of MetS, and patients with an increased waist circumference had more components of the MetS diagnostic criteria.[8] In the present study, spinal BMD was significantly lower in patients with than without MetS ($p = 0.033$). Additionally, the mean femoral neck BMD T score was significantly higher in patients with than without MetS ($p = 0.002$). There was no difference in the mean total femoral BMD T score.

We found no difference in the ages at menopause and menarche between patients with and without MetS in the present study. However, BMI, blood pressure, fasting blood sugar, spinal BMD, and femoral neck BMD were significantly different between the two groups. Conversely, there was no difference in the hemoglobin level or total femoral BMD between patients with and without MetS. However, the mean age of the patients

was significantly higher in patients with than without MetS ($p = 0.033$).

Joo et al.[9] investigated the incidence of MetS and the serum uric acid levels of premenopausal and postmenopausal women and diagnosed MetS in 7.45% (63/846) of the premenopausal women and 23.87% (333/1395) of the postmenopausal women. The triglyceride, free fatty acid, LDL, fasting glucose, uric acid, and insulin levels; BMI; and blood pressure were higher in the postmenopausal than premenopausal women. The serum uric acid level was significantly higher in patients with MetS in both groups, but there was no difference between the premenopausal and postmenopausal patients in the MetS group. Additionally, age and the serum uric acid level were associated with MetS.[9]

Özelçi et al.[10] retrospectively investigated the relationship between BMD and MetS in postmenopausal women and found that 29% of the patients had MetS. The women with MetS were significantly older than those without MetS. The BMI; waist circumference; diastolic and systolic blood pressure; and fasting blood sugar, triglyceride, and calcium levels were significantly higher and the HDL cholesterol level was lower in patients with than without MetS. Furthermore, the number of smokers was significantly higher in the MetS group. The femoral neck T score was significantly higher in patients with than without MetS, but there was no difference in the BMDs among the lumbar vertebrae. However, the lumbar BMD was significantly higher in the patients with low HDL cholesterol levels.[10] von Muhlen et al.[11] reported that women with MetS had higher vertebral BMD, and although MetS is a protective factor against osteoporosis, women with MetS had more nonvertebral fractures in their study of 671 women. Hwang and Choi[12] found that patients with MetS had lower BMD after covariate adjustment. Kim et al.[13] reported that the lumbar spine and proximal femur in women with MetS had lower BMDs than those in women without MetS, but no significant difference was present after covariate adjustment. Kinjo et al.[14] found that MetS was positively associated with BMD. El Maghraoui et al.[15] also reported that MetS was positively correlated with BMD.

In the present study, we found no relationship between vasomotor symptoms and the spinal, femoral neck, and total femoral BMD. Tural et al.[16] compared the BMD of 79 postmenopausal women with (58%) and without (42%) vasomotor symptoms. BMD of the vertebrae and femoral neck was significantly lower in patients with than without vasomotor symptoms.[16] Crandall et al.[17] found no significant relationship of BMD with vasomotor symptom severity. However, vasomotor symptom severity was inversely associated with femoral neck and lumbar spinal vertebral BMD ($p = 0.004$ and $p = 0.045$, respectively). Gast et al.[18] found that women with severe vasomotor symptoms had significantly lower BMDs ($p = 0.0001$). In the present study, patients with and without osteopenia as shown by their spinal BMD measurements were evaluated according to their vasomotor symptom severity. Patients with severe, moderate, and no vasomotor symptoms were compared. No significant differences were found among these three groups. Patients with and without femoral neck osteopenia were also evaluated according to their vasomotor symptom severity. Patients with severe, moderate, and no vasomotor symptoms were compared. No significant differences were found among these three groups.

Ryu et al.[19] investigated the relationship between vasomotor symptoms and MetS in postmenopausal patients. The mean age of the patients was 54 years, and the patients had been menopausal for a mean of 4 years. The authors found that 58% of patients presented with vasomotor symptoms.

The presence of vasomotor symptoms was significantly associated with young age, a short menopausal period, high BMI, high waist circumference, and a poor lipid profile. In addition, the frequency of MetS was significantly higher in patients with vasomotor symptoms (22.2%) than without vasomotor symptoms (15.6%). Among patients with MetS, comparison of women with and without vasomotor symptoms showed that high HDL cholesterol and triglyceride levels were associated with vasomotor symptoms. In patients with MetS, the frequency of vasomotor symptoms significantly increased as the number of diagnostic components decreased.[19]

Hot flashes, the most common vasomotor symptom, can be explained by thermoregulatory events caused by menopausal changes including estrogen deficiency and estrogen surge.[20] Previous studies have shown that obesity may have a protective effect against vasomotor symptoms because of the higher endogenous estrogen activity.[21] However, recent studies have shown that obese women report more vasomotor symptoms than leaner women. A higher body fat ratio may cause these symptoms by increasing the patient's body temperature.[22,23] In addition, a relationship has been found between vasomotor symptoms and a high BMI and waist circumference. Thus, obesity can be considered a common factor of both MetS and vasomotor symptoms. Postmenopausal women with vasomotor symptoms generally have a worse lipid profile than women without symptoms.[22,24,25] In our study, no relationship between vasomotor symptom severity and BMI (>30 vs. <30 kg/m^2) was found among patients without MetS. We also found no relationship between BMI and vasomotor symptom severity among patients with MetS. The high triglyceride level in patients with MetS did not affect the severity of vasomotor symptoms. HDL cholesterol elevation did not affect vasomotor symptoms in patients either with or without MetS. Likewise, neither the fasting blood glucose level nor blood pressure affected vasomotor symptoms in patients with or without MetS.

Ryu et al.[19] found that high triglyceride and low HDL cholesterol levels were associated with vasomotor symptoms, but neither blood pressure nor fasting glucose were associated with vasomotor symptoms. Gast et al.[24] found that sweating was related to various metabolic components such as a high BMI, waist/hip ratio, and total cholesterol, LDL cholesterol, triglyceride, and glucose levels. We cannot say that postmenopausal sweating is present in all women because not all participants of their study were postmenopausal.[24] A study by Lee et al.,[26] which included 183 postmenopausal patients, showed a greater incidence of vasomotor symptoms in patients with than without MetS ($p = 0.034$). In addition, among patients with high triglyceride levels, as the number of MetS components increased, the severity of vasomotor symptoms also increased ($p = 0.039$, $p = 0.044$).[26] In a retrospective study conducted by Cagnacci et al.,[27] the ratio of total cholesterol to HDL cholesterol was associated with vasomotor symptoms ($p = 0.0001$). Triglyceride and glucose elevations were associated with vasomotor symptom severity ($p = 0.0001$ and $p = 0.0001$, respectively). However, there was no correlation between blood pressure and vasomotor symptoms.[27] In the present study, patients with and without MetS were grouped and compared according to the severity of vasomotor symptoms. There was no significant difference in the numbers of patients with and without MetS among those with severe vasomotor symptoms. However, among patients with moderate and no vasomotor symptoms, the number of patients with MetS was significantly lower than the number of patients without MetS ($p = 0.026$ and $p = 0.037$, respectively). In their study of 183 postmenopausal women, Lee et al.[26] found that

vasomotor symptoms occurred with higher frequency in patients with than without MetS. The limitations of their study were the small size of the groups, the absence of comparison with patients using hormone replacement therapy, and the absence of sufficiently objective criteria to assess vasomotor symptoms.

Conclusion

We found no relationship between BMD and vasomotor symptoms. Among patients with severe vasomotor symptoms, there was no significant difference between patients with and without MetS. However, among patients with moderate and no vasomotor symptoms, the number of patients with MetS was significantly lower than the number of patients without MetS. Future studies with larger study groups, newly postmenopausal patients (in terms of symptom severity), and efforts to more objectively assess symptoms will be useful.

Declaration of conflicting interest

The authors declare that there is no conflict of interest.

Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

References

1. Grady D. Clinical practice. Management of menopausal symptoms. *N Engl J Med* 2006; 355: 2338–2347. PubMed PMID: 17135587.
2. Reid R, Abramson BL, Blake J, et al. Managing menopause. *J Obstet Gynaecol Can* 2014; 36: 830–838 [in French, English abstract]. PubMed PMID: 25222364.
3. Stevenson JC, Crook D and Godsland IF. Influence of age and menopause on serum lipids and lipoproteins in healthy women. *Atherosclerosis* 1993; 98: 83–90. PubMed PMID: 8457253.
4. Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. Executive summary of the third report of The National Cholesterol Education Program (NCEP) expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (adult treatment panel III). *JAMA* 2001; 285: 2486–2497. PubMed PMID: 11368702.
5. Kozan O, Oguz A, Abaci A, et al. Prevalence of the metabolic syndrome among Turkish adults. *Eur J Clin Nutr* 2007; 61: 548–553. PubMed PMID: 17119546.
6. Freeman EW, Sammel MD, Lin H, et al. Duration of menopausal hot flushes and associated risk factors. *Obstet Gynecol* 2011; 117: 1095–1104. PMID: 21508748
7. Alberti KG, Eckel RH, Grundy SM, et al. Harmonizing the metabolic syndrome: a joint interim statement of the International Diabetes Federation Task force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity. *Circulation* 2009; 120: 1640–1645. PubMed PMID: 19805654.
8. Jouyandeh Z, Nayebzadeh F, Qorbani M, et al. Metabolic syndrome and menopause. *J Diabetes Metab Disord* 2013; 12: 1. PubMed PMID: 23497470. Pubmed Central PMCID: PMC3598172.
9. Joo JK, Hong GP, Han SE, et al. The association between serum uric acid level and incidence of metabolic syndrome according to menopausal status in Korean women. *J Menopausal Med* 2014; 20: 126–132. PubMed PMID: 25580424. Pubmed Central PMCID: PMC4286657.
10. Ozelci R, Dilbaz B, Ozkaya E, et al. Association between bone mineral density and metabolic syndrome in Turkish women who were postmenopausal. *Int J Gynaecol Obstet* 2016; 133: 370–374. PubMed PMID: 26868072.
11. von Muhlen D, Safii S, Jassal SK, et al. Associations between the metabolic syndrome and bone health in older men and

women: the Rancho Bernardo study. *Osteoporos Int* 2007; 18: 1337–1344. PubMed PMID: 17492393.
12. Hwang DK and Choi HJ. The relationship between low bone mass and metabolic syndrome in Korean women. *Osteoporos Int* 2010; 21: 425–431.
13. Kim H, Oh HJ, Choi H, et al. The association between bone mineral density and metabolic syndrome: a Korean population-based study. *J Bone Miner Metab* 2013; 31: 571–578.
14. Kinjo M, Setoguchi S and Solomon DH. Bone mineral density in adults with the metabolic syndrome: analysis in a population-based U.S. sample. *J Clin Endocrinol Metab* 2007; 92: 4161–4164. PubMed PMID: 17785365.
15. El Maghraoui A, Rezqi A, El Mrahi S, et al. Osteoporosis, vertebral fractures and metabolic syndrome in postmenopausal women. *BMC Endocr. Disord* 2014; 14: 93.
16. Tural A, Yoldemir T and Erenus M. Assessment of bone mineral density should be considered earlier in perimenopausal women with vasomotor symptoms. *Int J Gynaecol Obstet* 2009; 107: 114–116. PubMed PMID: 19666170.
17. Crandall CJ, Aragaki A, Cauley JA, et al. Associations of menopausal vasomotor symptoms with fracture incidence. *J Clin Endocrinol Metab* 2015; 100: 524–534. PubMed PMID: 25522264. Pubmed Central PMCID: PMC4318890.
18. Gast GC, Grobbee DE, Pop VJ, et al. Vasomotor symptoms are associated with a lower bone mineral density. *Menopause* 2009; 16: 231–238. PubMed PMID: 19034053.
19. Ryu KJ, Park HT, Kwon DH, et al. Vasomotor symptoms and metabolic syndrome in Korean postmenopausal women. *Menopause* 2015; 22: 1239–1245. PubMed PMID: 25899005.
20. Freedman RR. Pathophysiology and treatment of menopausal hot flashes. *Semin Reprod Med* 2005; 23: 117–125. PubMed PMID: 15852197.
21. Campagnoli C, Morra G, Belforte P, et al. Climacteric symptoms according to body weight in women of different socio-economic groups. *Maturitas* 1981; 3: 279–287. PubMed PMID: 7334937.
22. Gast GC, Grobbee DE, Pop VJ, et al. Menopausal complaints are associated with cardiovascular risk factors. *Hypertension* 2008; 51: 1492–1498. PubMed PMID: 18391100.
23. Thurston RC, Sowers MR, Sutton-Tyrrell K, et al. Abdominal adiposity and hot flashes among midlife women. *Menopause* 2008; 15: 429–434. PubMed PMID: 18204407. Pubmed Central PMCID: PMC2875947.
24. Gast GC, Samsioe GN, Grobbee DE, et al. Vasomotor symptoms, estradiol levels and cardiovascular risk profile in women. *Maturitas* 2010; 66: 285–290. PubMed PMID: 20400247.
25. Park JK, Lim YH, Kim KS, et al. Body fat distribution after menopause and cardiovascular disease risk factors: Korean national health and nutrition examination survey 2010. *J Womens Health (Larchmt)* 2013; 22: 587–594. PubMed PMID: 23746280.
26. Lee SW, Jo HH, Kim MR, et al. Association between menopausal symptoms and metabolic syndrome in postmenopausal women. *Arch Gynecol Obstet* 2012; 285: 541–548. PubMed PMID: 21853251.
27. Cagnacci A, Cannoletta M, Palma F, et al. Menopausal symptoms and risk factors for cardiovascular disease in postmenopause. *Climacteric* 2012; 15: 157–162. PubMed PMID: 22141325.