# Is metabolic syndrome related to postmenopausal osteoporosis? A retrospective study

## Metabolik sendrom postmenopozal osteoporoz ile ilişkili midir? Retrospektif bir çalışma

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#### Abstract

Aim: To evaluate the difference between postmenopausal women with and without osteoporosis in terms of **Disease, Medical School** Yozgat, Turkey.

Methods: A total of 98 postmenopausal women younger than 65 years, were enrolled in the study. According to the bone mineral density examination; 49 participants who had T-score>-2.5 at the spine or/and femoral neck were included in the group without osteoporosis (Group 1), and 49 participants who had T-score<-2.5 at the spine or/and femoral neck were included in the osteoporosis group (Group 2). Patient's profile which included all demographic data, particularly anthropometric evaluation and medical history was obtained. Serum fasting glucose, lipid profiles and 25 OH vitamin D levels were also recorded.

Results: Age (p=0.001), menopausal age (p=0.003), systolic blood pressure (p=0.004) and diastolic blood pressure (p=0.001) of Group 2 were significantly higher than Group 1. There were no significant difference in terms of body mass index, weight, lipid profiles, serum calcium and serum 25 OH vitamin D levels among the groups (p>0.05 for all). Twenty five (51%) of 49 women in Group 1 and 36 (73%) of 49 women in Group 2 had metabolic syndrome. There was a statistically significant relationship between osteoporosis and the metabolic syndrome (p=0.037).

Conclusion: Our results demonstrated that osteoporosis is related with the metabolic syndrome in postmenopausal women.

Keywords: Metabolic syndrome, menopause, osteoporosis.

#### Öz

Amaç: Postmenopozal kadınlarda, osteoporoz ile metabolik sendrom arasındaki ilişkiyi değerlendirmek.

Yöntemler: 65 yaşın altında toplam 98 postmenopozal kadın çalışmaya dahil edildi. Kemik mineral dansitometre sonucuna göre; lumber ve/veya femur boyun T skoru>-2.5 olan 49 hasta postmenopozal osteoporoz olmayan gruba (Grup 1), T skoru<-2.5 olan 49 hasta postmenopozal osteoporoz grubuna (Grup 2) dahil edildi. Tüm demografik verileri içeren hasta profili, antropometrik değerlendirme ve tıbbi öykü kaydedildi. Serum açlık glukozu, lipit profili ve serum 25 OH D vitamin seviyesi de kaydedildi.

Bulgular: Grup 1 ve Grup 2 karşılaştırıldığında; yaş (p=0.001), menopoz yaşı (p=0.003) sistolik kan basıncı (p=0.004) ve diyastolik kan basıncı (p=0.001) Grup 2'de Grup 1'e göre anlamlı şekilde daha yüksekti. Vücut kitle indeksi, boy, kilo, lipid profili, serum 25 OH vitamin D düzeyleri açısından gruplar arasında anlamlı fark yoktu (p>0.05). Osteoporozu olan 49 hastanın 36'sında (%73), osteoporozu olmayan 49 hastanın ise 25'inde (%51) metabolik sendrom tespit edildi. Osteoporoz ile metabolik sendrom arasında istatistiksel olarak anlamlı ilişki tespit edildi (p=0.037).

Sonuç: Postmenopozal kadınlarda osteoporoz ile metabolik sendrom arasında anlamlı ilişki olduğu tespit edilmiştir.

Anahtar Kelimeler: Metabolik sendrom, menopoz, osteoporoz.

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Ethics Committee Approval: The study wass approved by the local ethical authority.

Etik Kurul Onayı: Çalışma lokal etik komite tarafından onaylanmıştır.

Conflict of Interest: No conflict of interest was declared by the authors.

Çıkar Çatışması: Yazarlar çıkar çatışması bildirmemişlerdir.

Financial Disclosure: The authors declared that this study has received no financial support. Finansal Destek: Yazarlar bu çalışma için finansal destek almadıklarını beyan etmişlerdir.

Geliş Tarihi / Received: 30.04.2018 Kabul Tarihi / Accepted: 30.06.2018 Yayın Tarihi / Published: 20.07.2018

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# Introduction

Metabolic syndrome is a cluster of systemic disorders and is well known to increase the risk of endocrinopathy. Insulin resistance plays a central role and is related to the all components of metabolic syndrome, defined by the presence of central obesity, dyslipidemia, glucose intolerance or diabetes mellitus, and hypertension [1]. National Cholesterol Education Program's Adult Treatment Panel III (NCEP-ATP III) criteria and International Diabetes Federation (IDF) criteria are used for diagnosis of metabolic syndrome [2]. According to the ATP III criteria, metabolic syndrome is reported to be present in 30% of men and 41.8% of women in Turkey [3]. The same study also showed an increase in the prevalence of the metabolic syndrome, especially over the age of 45 years.

Osteoporosis is one of the most common diseases worldwide. Due to its prevalence, osteoporosis is considered as an important public health concern. Approximately 30% of all postmenopausal women have osteoporosis in the United States and in Europe [4]. Osteoporosis and cardiovascular disease are age-related conditions that affect mortality and morbidity. The relation of coronary artery atherosclerosis and calcification with osteoporosis is reported in women [5]. Atherosclerosis and hyperlipidemia were also reported to be associated with osteoporosis [6].

The data about the association between osteoporosis and the metabolic syndrome is limited [7, 8]. There is no data in the literature, concerning the relation of postmenopausal osteoporosis and metabolic syndrome in Turkish population. Therefore, we aimed to probe the relation of osteoporosis and metabolic syndrome in postmenopausal women.

# **Material and Methods**

The study was approved by Bozok University ethics committee. All procedures were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008 and informed consent was obtained from all participants for being included in the study. Written consent could not be taken due to the retrospective design of the study.

A total of consecutive 98 postmenopausal women who were younger than 65 years living in Yozgat area/Turkey were enrolled in the study between January 2016 and January 2017. All participants were postmenapousal for at least one year. Patients suffering from ischemic heart disease, chronic systemic inflammatory disorders, patients with renal failure, patients suffering from thyroid and parathyroid related disorders and patients above 65 years of age were excluded from the study.

Participants were assigned in two groups based on their bone mineral density (BMD) score; 49 participants who had T-score>-2.5 at the spine or/and femoral neck were included in the group without osteoporosis (Group 1) and 49 participants who had T-score  $\leq$ -2.5 at the spine or/and femoral neck were included in the osteoporosis group (Group 2).

Personal medical history, including age and menopause duration was obtained. Weights (kg) and heights (m) of the participants were measured. Body mass index (BMI) as  $kg/m^2$ 

was calculated by the formula of (weight in kg) / (height in meters<sup>2</sup>). Waist circumference (WC) of the participants was measured to evaluate abdominal obesity. Blood pressure (mmHg) was measured using with standard mercury manometer. The normal limit was 130 mmHg for systolic blood pressure and 85 mmHg for diastolic blood pressure, consistent with NCEP-ATP III cut points for blood pressure in the definition of the metabolic syndrome [2]. Patients taking antihypertensive medications were also classified as hypertensive. Blood samples for fasting glucose, serum calcium (mg/dL), 25 OH vitamin D (ng/mL) and lipid parameters including total cholesterol (mg/dL), HDL (mg/dL), LDL (mg/dL) and triglyceride (mg/dL) were centrifuged at room temperature for 5 minutes at 3000 RPM. The extracted serum was kept in ice bags and put in deep freezers at -80 °C.

Metabolic syndrome was defined with the NCEP ATP III criteria. This definition requires the presence of at least three or more of the five components of the following categorically defined risk factors: Abdominal obesity; waist circumference greater than 88 cm, hypertension (130/85 mmHg or greater, taking antihypertensive medications), high triglycerides (150 mg/dL or greater), low HDL cholesterol (less than 50 mg/dL in women), hyperglycemia (100 mg/dL or greater or taking antidiabetic medication) [2].

### Statistical analysis

The findings were analyzed statistically using the Statistical Package for the Social Sciences, version 18.0 (Chicago, IL). The distribution was evaluated with the Shapiro-Wilk test. Continuous variables were expressed as mean  $\pm$  standard deviation and non-normally distributed variables were expressed as median with minimum and maximum values. Mean values of the two groups were compared by independent samples T test for variables distributed normally and Mann-Whitney U-test for variables distributed non-normally. Chi square test was used for categorical variables. The value of p < 0.05 was considered statistically significant.

# Results

Descriptive characteristics are summarized in Table. When compared with Group 1, mean age  $(54.5\pm5.7 \text{ vs. } 58.2\pm4.6; p=0.001)$ , menopausal duration [7 (1-20) vs. 10 (1-24); p=0.003)], systolic blood pressure (121.1±10.9 vs. 128.7±13.7; p=0.004) and diastolic blood pressure (76.7±7.8 vs. 81.7±7.8; p=0.001) were significantly higher in Group 2. Lumbar spine BMD (-1.68±0.59 vs. -3.03±0.49; p=0.001) and femur neck BMD (-1.19±0.65 vs. -1.95±0.84; p=0.001) were significantly lower in Group 2.

There were no significant difference between the groups in terms of menopause age (p=0.997), weight (p=0.324), height (p=0.388), BMI (p=0.541), fasting glucose (p=0.539), total cholesterol (p=0.628), HDL (p=0.444), LDL (p=0.732), triglyceride (p=0.198), and serum 25 OH vitamin D (p=0.707) levels (Table).

The prevalence of the metabolic syndrome was 62% (61 of 98 participants) in all study population. The metabolic syndrome was detected in 25 (51%) of 49 participants and 36 (73%) of 49 participants in Group 1 and Group 2, respectively.

There was a statistically significant relationship between osteoporosis and the metabolic syndrome (p=0.037). Table: Descriptive features

Parameter	Group 1 (n=49)	Group 2 (n=49)	р
Age (year) $\beta$	54.5±5.7	58.2±4.6	0.001
Height (m) <sup><math>\beta</math></sup>	$1.56 \pm 0.06$	$1.55 \pm 0.05$	0.388
Weight (kg) <sup>β</sup>	80.4±12.1	78.0±12.6	0.324
Body mass index $(kg/m^2)^{\beta}$	32.9±5.3	32.2±5.5	0.541
Waist circumference (cm) $^{\beta}$	103.4±12.3	104.8±10.6	0.523
Lumbal spine BMD $(g/cm^2)^{\beta}$	$-1.68\pm0.59$	$-3.03\pm0.49$	0.001
Femur neck BMD (g/cm <sup>2</sup> ) <sup>β</sup>	-1.19±0.65	$-1.95 \pm 0.84$	0.001
Menopause age (year) <sup><math>\beta</math></sup>	47.3±6.2	47.9±3.9	0.997
Menopausal duration $(year)^{\mu}$	7 (1-20)	10 (1-24)	0.003
Fasting glucose (mg/dL) <sup>µ</sup>	101 (71-	109 (73-	0.539
	310)	301)	
Total cholesterol (mg/dL) $^{\beta}$	203.7±35.6	207.6±42.4	0.628
HDL (mg/dL) <sup><math>\beta</math></sup>	51.0±10.6	52.8±11.0	0.444
LDL (mg/dL) <sup><math>\beta</math></sup>	123.4±30.7	125.7±33.4	0.732
Triglyceride $(mg/dL)^{\beta}$	127(39-427)	143 (57-	0.198
		451)	
Serum calcium (mg/dL) $^{\beta}$	9.5±0.5	9.5±0.4	0.824
25 OH vitamin D (ng/mL) <sup><math>\mu</math></sup>	14 (4-68)	14 (4.1-134)	0.707
Mean sistolic pressure			
(mm/Hg) <sup>β</sup>	121.1±10.9	128.7±13.7	0.004
Mean diastolic pressure			
(mm/Hg) <sup>β</sup>	76.7±7.8	81.7±7.8	0.001
Metabolic syndrome (n (%))	25 (51%)	36 (%73)	0.037

 $\beta$ : mean  $\pm$  standard deviation,  $\mu$ : median and range

# Discussion

In this study, a significant relation has been found between metabolic syndrome and osteoporosis in postmenopausal women.

Obesity is commonly seen in postmenopausal women. Silva et al. reported that about 50% of postmenopausal women are obese [9]. Previous studies have demonstrated that body fat mass and BMI were higher in postmenopausal women than perimenopausal women [10]. In this study, mean BMI in both groups were above 30 kg/m2 as obese. However, there were no significant differences in BMI, WC and weight between the groups.

A several number of studies have supported that osteoporosis and cardiovascular diseases have a link because of common pathophysiological and genetic risk factors [11-13]. Recent studies also proved that estrogen deficiency is an independent risk factor for osteoporosis and coronary heart disease [12, 13]. Estrogen level has been found to be positively correlated with BMD and HDL [14, 15]. Barengolts et al. compared the lipid profile in postmenopausal women with and without osteoporosis [16]. No significant difference was found between the groups. Same as the literature, in our study, there was no significant difference in lipid profiles in postmenopausal women with and without osteoporosis. On the other hand, the prevalence of both cardiovascular disease and osteoporosis increase with advanced age [17]. All postmenopausal patients included the study were under 65 years of age, because the risk of cardiovascular disease was expected to increase with age progression, especially above 60.

The components of metabolic syndrome, such as high blood pressure, increased triglycerides, and reduced HDL are also related to osteoporosis while other components such as obesity are not. It is demonstrated that osteoporosis is related to inflammation. It was recently shown that, participants with high insulin resistance have more inflammation than participants with low insulin resistance [18, 19]. Some studies advocated that low chronic inflammation may affect bone health [20]. According to a study, the prevalence of DM and insulin resistance in postmenopausal women was higher than in premenopausal women [21]. Gundoğan et al. reported that women who were between 50-59 ages had higher prevalence of the metabolic syndrome than normal population [3]. They found the metabolic syndrome rate as 40.4%, according to NCEP-ATP III criteria and as 48.3% according to IDF criteria. The impact of risk factors of the metabolic syndrome on bone health has been regarded as controversial in the literature [22-24].

A study showed that there was an association between metabolic syndrome features and prevalent osteoporotic fractures in a cross-sectional analysis, and metabolic syndrome was related to lower BMD [24]. The opposite results have also been reported [22, 23]. Especially in some studies, the authors suggested that obesity, diabetes and the metabolic syndrome have protective effects for osteoporosis [22]. On the other hand, a meta-analysis indicated that the metabolic syndrome is associated with a 15% reduced risk of fractures in adults [23].

In the present study, the rate of the metabolic syndrome was higher in patients with osteoporosis. Also mean systolic and diastolic blood pressures were higher in patients with postmenopausal osteoporosis. Sedentary lifestyle can potentially contribute to insufficient sun exposure and individual components of metabolic syndrome. Age of the patients with postmenopausal osteoporosis was significantly higher than the patients without postmenopausal osteoporosis. Therefore, we thought that significant differences in the prevalence of the metabolic syndrome between the groups may be related to higher age, and also sedentary lifestyle in the postmenopausal osteoporosis group.

Our study has several limitations; because of crosssectional study design, we cannot assess reasons between metabolic syndrome and low BMD. Secondly, our group consists of female patients who refer to the endocrine clinic. Population generalization cannot be done because it does not include male patients.

In conclusion, in our study, the prevalence of the metabolic syndrome was found to be higher as 62% in all the postmenopausal participants. Our result showed that rate of the metabolic syndrome was higher in patients with osteoporosis than the patients without osteoporosis in the postmenopausal patients under 65 years of age.

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