Investigation of the risk factors associated with osteoporosis in postmenopausal women

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Abstract

Objective: Osteoporosis is a substantial global public health issue. The objective of this study was to evaluate the risk variables associated with osteoporosis among patients seeking care at an outpatient menopausal clinic in a tertiary university hospital.

Material and Methods: In this retrospective, cross-sectional study postmenopausal women who attended the outpatient menopause clinic of Başkent University Hospital between June 01, 2014, and August 31, 2015, were enrolled. Patients' datasheets were reviewed and data including age, body mass index, parity, duration and age of menopause, history of smoking and oral contraceptive pills (OCPs) use, natural or surgical menopause, and calcium-containing food consumption were collected through a standardized questionnaire. Bone mineral density (BMD) was measured at the femur neck and lumbar spine by dual energy X-ray absorptiometry.

Results: A total of 1,148 women with a mean age of 53.5±6.7 years, mean duration of menopause 7.1±6.2 years and mean age of menopause 46.3±5.1 years were identified. Of these, 235 (20.5%) were diagnosed as having osteoporosis. The average femur and lumbar T-values showed a decrease in normal weight patients compared to overweight, obese, and morbidly obese patients ($F=22,337$, $p<0.001$ and $F=50,195$, $p<0.001$, respectively). The mean femur T-values were higher in participants who used OCPs, regularly consumed a calcium-rich diet, and performed regular physical activity ($p<0.05$, $p<0.01$ and $p<0.05$). Positive correlations were noted between giving birth and femur T-values ($r=0.065$, $p=0.027$), between natural menopause and lumbar T-values ($r=0.060$, $p=0.043$), and between consuming a calcium-rich diet and femur T-values ($r=0.087$, $p=0.003$ and $r=0.064$, $p=0.031$, respectively).

Conclusion: Using OCPs, lifelong physical activity, and a healthy diet rich in calcium are important factors for the prevention of low lumbar spine and femoral BMD and by implication, osteoporosis. (J Turk Ger Gynecol Assoc 2023; 24: 235-40)

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Introduction

Menopause is defined as the onset of cessation of ovarian endocrine functions that marks the end of the reproductive years. For most women, menopause occurs between the ages of 45 and 55 as a natural consequence of biological aging due to the loss of follicular function and a decline in estrogen production. As stated by the World Health Organization (WHO), natural menopause is considered to have occurred after 12 months of uninterrupted menstrual cessation without any other apparent physiological or pathological cause or clinical intervention. In some women, "premature menopause" may occur earlier, before the age of 40 years, due to certain chromosomal abnormalities, autoimmune diseases, or other unknown causes. Menopause can also be caused by surgical or medical procedures. In the developed world, with increased life expectancy during the last century, an increasing number

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of women spend more than 20 years in the menopausal period (1,2).

Osteoporosis is among one of the most frequently encountered consequences of estrogen deprivation, substantially impairing the quality of life, and therefore strategies aimed at prevention of bone loss are of importance. Studies indicate that 20% of bone loss may occur during this period and about one in every 10 women is affected by osteoporosis worldwide. Osteoporosis, features of which are very low bone mineral density (BMD) and bone fragility, is characterized by deterioration in the micro- and macro-architecture of the bone tissue. Postmenopausal osteoporosis may frequently lead to bone fractures which are associated with severe pain, reduced mobility, and functional loss (3,4). Among the most widely applied techniques to measure bone density is dual-energy X-ray absorptiometry (DEXA). It is the gold standard technique to diagnose osteopenia and osteoporosis and assessment of the femur neck and lumbar spine are usually recommended by this technique (5).

Osteoporosis is a multifactorial disease in which genetics and environmental conditions play an important role. Like other multifactorial diseases, quantitative phenotype changes occur with the interaction of genotype and environment. It has been well-documented that osteoporosis is affected by environmental factors, such as smoking, diet, physical activity, sunlight, and the use of oral contraceptive pills (OCPs) (6-8). The Food and Drug Administration (FDA) in the USA has authorized a statement regarding the preventative effects of calcium-rich foods on bone health (6,7). The interest in the function of nutrition for the prevention and pathogenesis of osteoporosis is progressing. Recent evidence strongly suggests that while an unhealthy diet results in an increased risk of osteoporosis, a healthy dietary pattern plays a protective role. After all, nutrition is a modifiable factor that plays a role in both building bone mass and preventing osteoporosis. Among the nutrients demonstrated to protect against impaired bone health are calcium, phosphorus, magnesium, and adequate vitamin intake, especially vitamin D. In addition, food that have a positive effect on BMD include milk, dairy products, and red meat rich in fiber and protein (8).

In the bone health report published by the FDA, the importance of physical activity was emphasized at the very beginning. Physical activity and adequately consumed calcium and vitamin D, as part of a well-adjusted diet, may prevent the occurrence of osteoporosis and may build and maintain good bone health (9). Exercise has a substantial effect on BMD and it has been suggested that bone tissue can perceive biomechanical stress by means of an internal "mechanostat" and regulates its remodeling accordingly by increasing bone deposition (10). Mechanical usage (MU) determines bone mass by influencing bone remodeling. Reduced MU decreases new bone formation and increases bone loss near the bone marrow. Acute and chronic pauses in MU can affect the anatomical and tissue dynamic patterns of the bone, leading to postmenopausal osteoporosis similar to that seen in other forms of osteoporosis. Return to a normal MU stops bone loss through remodeling and enables the available bone to start remodeling increasing protection against osteopenia and osteoporosis (10).

Postmenopausal women are subject to primary osteoporosis as a result of estrogen deprivation. It is recommended that, in addition to physical activity, nutrition and a well-balanced diet are important tools for osteoporosis prevention and ameliorate bone health problems at older ages (8). Likewise, the use of hormone replacement therapy, antiresorptive therapy, and use of calcium-bearing substances during menopause is considered to contribute to a reduction in the risk of osteoporosis (11,12). In the modern world, with increased life expectancy, osteoporosis and osteoporosis-related fractures have become a public health problem that increases mortality and morbidity, especially in menopausal women, placing significant burdens on health resources. The aim of this study was to investigate the osteoporosis-related risk factors in patients who attended the outpatient menopause clinic of the Başkent University Hospital.

Material and Methods

In this cross-sectional, retrospective study, postmenopausal women who attended the Menopause Outpatient Clinic of Başkent University, Training and Research Center, Adana, between June 01, 2014, and August 31, 2015 were enrolled. The datasheets of all patients who were admitted to the outpatient menopause clinic during the study period were screened. Patients with medical disorders that could lead to osteoporosis or fractures, including parathyroid gland or adrenal gland disorders, and those receiving long-term steroids or low molecular weight heparins were excluded. The Başkent University Institutional Review Board provided ethical approval for the present research (approval number: KA22-505, date: 04.01.2023) and the study was conducted according to the principles of the Helsinki Declaration.

All anthropometric measurements of the patients were assessed and recorded. Body mass index (BMI) is calculated by dividing weight in kg by height in meters squared. BMD measurement was done using a Hologic QDR 4500 DEXA scanner device (Hologic, Boston, MA, USA). Measurements included the femoral neck and lumbar spine. According to the WHO criteria, a T-score of $\leq$-2.5 was defined as "osteoporosis", a T-score between -1.0 and -2.5 was defined as "osteopenia" and a T-score of $>$-1.0 was defined as "normal" (5).

Regular physical exercise was defined as doing exercises at least 3 days a week, at least 30 minutes daily. Regular consumption of a calcium-rich diet was defined as 2-4 servings of dairy daily including 240 mL of milk or yoghurt or 40-60 g of cheese (13). Data regarding the sociodemographic characteristics, lifestyle characteristics, obstetric data and menopause characteristics, medication use, history of fractures and relevant family history of the patients were gathered by a questionnaire prepared by the researchers in the light of the literature.

Statistical analysis

Descriptive statistics, given as mean and standard deviation or frequency and proportions, were calculated to describe the data. Two Independent samples t-test and the Mann-Whitney U test were used for comparisons between paired groups. For comparisons of three or more groups One-Way ANOVA analysis of variance was used, and to determine the difference between the groups a post-hoc Least Significant Difference test was used. Spearman's correlation analysis was performed to investigate the relationship between various pre-menopausal and menopausal factors that may have an effect on osteoporosis as defined by BMD measurements of the participants. For all tests, $p<0.05$ was considered significant.

Results

A total of 1,148 menopausal women with a mean age of 53.5±6.7 years (range; 34-82 years), a mean age at menopause of 46.3±5.1 years (range; 26-64 years), and a mean duration of menopause of 7.1±6.2 years (range; 1-35 years) were retrospectively reviewed (Table 1). While 1,017 (88.6%) of the patients were in natural menopause, 131 (11.4%) were in surgical menopause. Of the patients, 193 (16.8%) consumed calcium-rich foods, and 160 (13.9%) performed regular physical activity at least 3 days a week. Thirty (2.6%) of the patients had a history of fracture (osteoporotic fracture/fragility fracture) and 56 (4.9%) had a family history of fracture.

The mean height was 156.9±5.9 cm, the mean body weight was 72.6±12.4 kg, and the mean BMI was 29.4±5.1 kg/m^2. Based on BMI, 213 (18.6%) were defined as normal weight, 445 (38.8%) were overweight, 454 (39.5%) were obese (39.5%) and 36 (3.1%) were morbidly obese (3.1%). Of the patients, 143 (12.5%) did not use any contraceptive method. Among the patients who used contraception, 899 (78.3%) used non-hormonal methods such as intrauterine device and condom, and 106 (9.3%) used OCPs. Of the women 1077 (93.8%) were parous and 71 (6.2%) had never been pregnant. The mean gravida was 4.8±2.9, and the mean number of parity was 3.2±2.0.

Based on femoral T-values, 52.3% of the patients were in the normal range, whereas 42.8% had osteopenia and 4.9% were found to have osteoporosis. However, for lumbar T-values, 31.4% of the patients were in the normal ranges, while 48.2% were osteopenic and 20.5% were osteoporotic (Table 2). A further comparison of normal, overweight, obese, and morbidly obese women according to obstetric and anthropometric data is presented in Table 3. When women were compared for BMD values according to the contraceptive methods they used, the mean femur T-values were found to be significantly higher among women who had used OCPs ($p=0.040$, and $p=0.035$, respectively) (Table 4). No difference was found in mean lumbar T-values according to OCP use.

In pairwise comparisons according to the type of menopause, compared to the surgical menopause group, the mean lumbar BMD values were significantly higher in the natural menopause group (0.86±0.12 vs. 0.88±0.16; $p=0.041$) (Table 5). The mean lumbar T-value was significantly higher in natural menopausal group (-1.45±1.26) than in surgical menopause group (-1.70±1.09), ($t=2.395$, $p=0.018$). The mean femur T-values were significantly higher in those who regularly consumed calcium-rich foods (-0.73±1.07) compared with those who did not consume calcium-rich foods (-0.92±1.0), ($t=-2.359$, $p=0.018$). The mean femur T-values were found to be significantly higher in those who engaged in regular physical activity (0.77±1.14) than in those who did not (0.74±1.13), ($t=-2.496$, $p=0.013$). No statistically significant difference was found between smoking, hormone replacement and antiresorptive therapy, calcium use, and any of the BMD measurements.

Spearman correlation analysis identified several significant correlations, including weak positive correlations between femur T- and gravida and parity ($r=0.065$, $p=0.027$ and $r=0.092$, $p=0.002$, respectively). While a statistically significant positive correlation was demonstrated between natural menopause and lumbar T-values ($r=0.060$, $p=0.043$), a significant positive

Table 1. Anthropometric characteristics of the study population

Variable	Mean ± SD	Range
Age, years	53.5±6.7	34-82
Age at menopause, years	46.3±5.1	26-64
Duration of menopause, years	7.1±6.2	1-35
BMI (kg/m^2)	29.4±5.1	17.2-55.7

SD: Standard deviation, BMI: Body mass index

Table 2. Bone mineral density measurements of the study population and their stratification according to T-values

Area of BMD measurement	Normal, (n, %)	Osteopenia, (n, %)	Osteoporosis, (n, %)
Femur T-value	600 (52.3%)	492 (42.8%)	56 (4.9%)
Lumbar spine T-value	360 (31.4%)	553 (48.2%)	235 (20.5%)

BMD: Bone mineral density

Table 3. Comparison of normal, overweight, obese and morbidly obese women with a reference to anthropometric data

Patient characteristics and BMD measurements	Normal, (n=213), (mean ± SD)	Overweight, (n=445), (mean ± SD)	Obese, (n=454), (mean ± SD)	Morbid obese, (n=36), (mean ± SD)	F	p
Age (years)	51.6±6.5	53.3±6.6	54.3±6.8	56.7±6.5	**10,817**	<0.001
Gravida (n)	3.6±2.2	4.8±3.0	5.3±2.8	5.8±3.8	**18,842**	<0.001
Parity (n)	2.2±1.4	3.0±2.0	3.7±2.1	4.1±2.7	**28,798**	<0.001
Menopause age (years)	44.8±5.2	46.4±4.8	46.9±4.9	47.0±7.0	**8,590**	<0.001
Duration of menopause (years)	6.7±5.6	6.8±6.1	7.3±6.3	9.7±8.9	**2,864**	**0.036**
Femur T-value	-1.379±0.93	-1.055±0.89	-0.560±1.02	-0.046±0.98	**50,195**	<0.001
Lumbar T-value	-1.755±1.25	-1.607±1.16	-1.282±1.26	-0.849±1.39	**12,282**	<0.001

BMD: Bone mineral density, SD: Standard deviation, *One-Way ANOVA test

Table 4. Comparison of dansitometric measurements according to the contraceptive methods used during the reproductive ages

Area of BMD measurement	No contraceptive method, (n=143)	Non-OCP method, (n=899)	OCP use, (n=106)	F	p
Femur T-value	-0.8821±0.970	-0.9171±1,007	-0.6465±1,133	**3,370**	**0.035**†
Lumbar T-value	-1.5267±1,277	-1.5062±1,234	-1.2168±1,255	2,681	0.069

BMD: Bone mineral density, OCP: Oral contraceptive pills, *One Way ANOVA test, †p<0.05

Table 5. The correlations between BMD values and obstetric data, menopause status, medication use, and lifestyle characteristics

Variation	Spearman's rho	Femur T-value	Lumbar T-value
Gravida	r	**0.065***	-0.035
	p	**0.027**	0.231
Parity	r	**0.092****	-0.022
	p	**0.002**	0.456
Natural menopause	r	0.030	**0.060***
	p	0.315	**0.043**
Premature menopause	r	-0.055	-0.042
	p	0.063	0.158
Hormone replacement therapy	r	-0.018	-0.023
	p	0.553	0.430
Antiresorptive therapy	r	-0.019	0.031
	p	0.520	0.295
Calcium preparation	r	0.006	0.029
	p	0.849	0.321
Smoking	r	-0.019	0.009
	p	0.511	0.772
Regular consumption of calcium-rich food	r	**0.064***	0.022
	p	**0.031**	0.455
Practicing regular physical exercise	r	-0.044	0.009
	p	0.138	0.772

BMD: Bone mineral density, r: Spearman's rho. *Correlation is significant at the 0.05 level (2-tailed). **Correlation is significant at the 0.01 level (2-tailed)

correlation was found between consuming calcium-rich foods regularly and femur T-values (r=0.064, p=0.031). A positive, significant correlation was found between regular physical activity and femur T-values (r=0.076, p=0.010), (Table 5).

Discussion

In this cross-sectional, descriptive study enrolling a total of 1148 postmenopausal women who attended the outpatient menopause clinic of a tertiary university hospital, the mean femur BMD and T-values were higher in those who used OCPs during the pre-menopausal period, those who had natural menopause and those who consumed calcium-rich foods. In addition, the mean femur BMD values were found to be higher in those who were parous and performed regular physical activity.

İpek et al. (14) evaluated osteoporosis risk in 537 postmenopausal women aged 45 years and older. The the mean age was 59.5±8.6 years, the mean age at menopause was 49.0±3.4 years and the mean duration of menopause was 13.8±1.4 years. Lumbar T-values showed that 24.0% (n=129) were normal, 44.1% (n=237) were osteopenic and 31.8% (n=171) were osteoporotic. Again, different proportions were found when evaluating femur T-values: 40.2% (n=216) had normal BMD; 48.8% (n=262) were classified as osteopenic; and 11% (n=59) were osteoporotic (14). In the present study, the mean age of the patients was younger, and the mean age at menopause was lower, the duration of menopause was longer, and according to lumbar T-values, the rate of having a normal

BMD (31.4%) and osteopenia (48.2%) were lower, and the rate of osteoporosis (20.5%) was higher as compared to the study of İpek et al. (14).

In studies conducted in postmenopausal women, a significant relationship was shown between BMI and lumbar and femoral BMD values (15-17). According to our results, the mean femoral BMD and lumbar BMD values of the participants were significantly higher in overweight, obese, and morbidly obese women in comparison to those with normal weight. This result suggests that increased body weight can play a protective role against osteoporosis in postmenopausal women. However, in a study by Gürlek et al. (18), increased body weight showed a positive association with BMD, while increased waist circumference had a negative effect on BMD. Researchers have suggested that obesity may increase BMD values with mechanical effects, on the other hand abdominal obesity may dysregulate bone metabolism through systemic inflammation (18).

In a population-based study by Nguyen et al. (19) examining the relationship between lifestyle factors and BMD in the aged population, it was found that BMD was affected by calcium consumption and muscle strength. Femoral neck BMD measurement was about 5% higher in both men and women with higher quadriceps strength and calcium consumption, compared to those with lower muscle strength and lower calcium consumption (19). In the study by Ilesanmi-Oyelere and Kruger (8) investigating the relationship between nutrition and bone health in the postmenopausal period 127 women aged 54-81 years were enrolled. The study revealed a favorable link between the consumption of foods containing high levels of calcium, riboflavin, and phosphorus, and BMD in the lumbar region and femoral neck (8). In the present study, a significant but very weak positive correlation was found between a regular calcium-rich diet and femur BMD. The mean femur T-values were significantly higher in those who consumed calcium-rich foods compared to those not consuming calcium-rich foods.

A meta-analysis has shown evidence of the beneficial effects of exercise, specifically those involving varied impact loading characteristics, on the lumbar spine and femoral neck in elderly individuals (20). It was suggested that exercise can be an effective intervention for promoting bone morphogenesis in patients with osteoporosis (20,21). In the present study, we found mean femoral BMD was significantly higher in those who practiced regular physical activity as opposed to those who did not, and a significant but very weak positive correlation was noted between regular physical activity and femoral BMD.

In a systematic review of 75 studies, the effect of OCP use and hormone replacement therapy on BMD was assessed in premenopausal and perimenopausal women. A positive effect on BMD was demonstrated in perimenopausal women receiving OCPs (11). Studies have shown that this is particularly related to estrogen, which plays a critical role in bone homeostasis with well-known beneficial effects on bone mass, although the mechanism is not fully understood. In the context microenvironment, estrogen has a crucial role on osteoclastic and osteoblastic functions, preventing tonic bone turnover and sustaining bone formation and resorption balance. In a retrospective cohort study conducted on 110 perimenopausal Korean women older than 40 years, Kim et al. (22) concluded that the decrease in BMD in both the lumbar and femoral regions in the perimenopausal period was associated with active bone turnover, and that OCPs may prevent bone loss by suppressing bone turnover. In the present study, an assessment of the contraceptive methods used during the pre-menopausal period revealed that the mean femoral BMD values were higher in those who used OCPs compared to those who used non-OCP methods. There was a very weak positive correlation between giving birth and femoral T-values. This may be because of the use of regular calcium supplementation throughout the pregnancy as a part of national health policy. A study by Yaraman and Karaoğlan (23) investigating osteoporosis-related risk factors among postmenopausal women and revealed a significant relationship between age, daily calcium intake, menopause age, tea and coffee consumption, BMI, parity, and exercise and lumbar and femoral neck T-scores. Moreover, Schnatz et al. (24) found that multiparity and history of breast-feeding decreased the development of osteoporosis in postmenopausal women.

Study Limitations

Our study has some limitations. We calculated BMI by measuring height and weight, but we did not measure waist circumference. We also suggest that it would be more accurate to evaluate postmenopausal women in terms of osteoporosis risk by measuring waist circumference and calculating homeostasis model assessment of insulin resistance, a measure of insulin resistance, and to assess BMD measurements by considering other criteria of the metabolic syndrome. The strength of our study is the enrollment of a large study sample size. Since it is regional research with a large sample size, it provides useful regional data about osteoporosis. Despite the large sample size, due to being a single-center study, and reflecting the eating and exercising behaviors of a single region, the results cannot be extrapolated to the whole country. Further studies performed in various regions and conducted in a multi-center design would definitely contribute to the results of the current study.

Conclusion

This retrospective, cross-sectional study of a large sample revealed effects of OCP use during the fertile period, lifelong physical activity, and a healthy diet rich in calcium for the prevention of osteoporosis in the postmenopausal period. Given the increasing proportion of the aged population, osteoporosis and osteoporosis-related fractures have not only become an important public health concern, but also hamper the quality of life of the elderly. It is important to be aware of strategies to prevent or alleviate osteoporosis-related long-term consequences.

Ethics Committee Approval: *The Başkent University Institutional Review Board provided ethical approval for the present research (approval number: KA22-505, date: 04.01.2023) and the study was conducted according to the principles of the Helsinki Declaration.*

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