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Original Article

Association between osteoporosis and symptomatic knee osteoarthritis in postmenopausal women: A case-control study

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Abstract

Background: Postmenopausal women with symptomatic knee osteoarthritis (KOA) may be at increased risk of bone loss due to reduced physical activity. However, findings on the association between KOA and osteoporosis have been inconsistent. This study aimed to assess the relationship between symptomatic KOA and bone mineral density (BMD) in postmenopausal women.

Methods: Postmenopausal women with symptomatic KOA were recruited from a rheumatology clinic. KOA was diagnosed according to the American College of Rheumatology (ACR) criteria. Age-matched postmenopausal women without clinical KOA served as controls. BMD at the femoral neck (FN) and lumbar spine (LS) was measured using dual-energy X-ray absorptiometry (DXA). Osteoporosis was defined as a T-score < -2.5 at either site. Statistical analyses included Student's t-test, chi-square test, and multiple regression analysis. Data were analyzed using SPSS software.

Results: Seventy participants (35 KOA patients and 35 controls) with mean ages of 61.9±8.7 and 58.8±6.8 years, respectively (P = 0.67), were included. No significant differences in BMD were found between the groups. However, multiple regression analysis revealed that obesity was significantly associated with a reduced risk of osteoporosis (OR = 0.23; 95% CI: 0.058–0.945).

Conclusion: This study found no significant association between symptomatic KOA and osteoporosis in postmenopausal women. Interestingly, obesity appeared to have a protective effect against osteoporosis. Further large-scale, long-term studies are needed to confirm these findings and explore underlying mechanisms.

Keywords: Association, Knee osteoarthritis, Symptomatic postmenopausal women.

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Knee osteoarthritis (KOA) is a painful and disabling disease that can profoundly affect quality of life and physical function (1, 2). KOA is not a localized disease of cartilage but is considered a chronic disease of the entire joint, which may result from multiple pathophysiological mechanisms (2, 3). Osteoarthritis (OA) and osteoporosis are both common in postmenopausal women; these conditions in older adults may be leading causes of morbidity, mortality, and poor health status (2-4). Approximately 13% of women aged 60 years and older have symptomatic KOA, and 57.4% of them have osteoporosis at the femoral neck or lumbar spine (1-4). Local and systemic inflammation contribute to the development of pain and disease progression in OA (5). In women with OA, the risk of fracture is higher than in those without OA (6-8). Furthermore, patients with osteoarthritis, especially symptomatic KOA, have a higher risk of falling, and thus patients with osteoarthritis and osteoporosis together have a higher risk of fracture (9). Therefore, the association between symptomatic KOA and osteoporosis is of particular importance. However, the results of previous studies on this association have been contradictory, likely due to differences in study designs and characteristics (10–15).

These inconsistencies may reflect variations in the risk factors associated with KOA among study populations. Since some risk factors for KOA may have a protective effect against bone loss, the relationship between KOA and osteoporosis may partly depend on the distribution of these risk factors. A nonlinear, site-specific inverse association has been demonstrated between osteoporosis and KOA in subjects over 50 years of age (16). Similarly, an inverse relationship between osteoporosis and osteoarthritis of the hands, knees, and lumbar spine was found in participants in the Chingford's study (17). In contrast, there were no significant differences in bone mineral density (BMD) and osteoporosis in postmenopausal women with KOA aged 40–60 years compared with age-matched controls (10). In postmenopausal women with KOA, in addition to the usual osteoporosis risk factors, low physical activity due to pain may also contribute to bone loss and osteoporosis. For these reasons, people with lower extremity osteoarthritis are at increased risk of osteoporosis and bone fractures (11, 12, 16, 18-21). In particular, the risk of fracture is higher in patients with advanced KOA (11, 12). Since osteoarthritis, falls, and fragility fractures are common in older adults and that osteoporosis is more common in women, this study was designed to determine the association between symptomatic KOA and osteoporosis in postmenopausal women.

Methods

Participants in this study were recruited from patients visiting the rheumatology clinic of Rouhani Hospital in Babol, Iran. To be eligible for the study, subjects had to have symptomatic KOA with a history of knee pain of at least 3 months and a diagnosis of KOA confirmed by ACR clinical criteria (22).

Asymptomatic individuals without clinical KOA who did not meet ACR criteria and visited the same clinic for laboratory testing or bone densitometry were included as controls. Participants with a history of knee or hip surgery, spine surgery, osteoporotic fractures, those taking medications such as anti-osteoporosis drugs, especially vitamin D and calcium, within 3 months prior to the study, those taking corticosteroids, and those with a history of inflammatory arthritis or septic arthritis were excluded. A similar set of exclusion criteria was applied to the control group. Bone mineral density (BMD) at the femoral neck (FN) and lumbar spine (LS) was assessed by dual-energy x-ray absorptiometry (DXA) using a Hologic densitometer and results were expressed as BMD g/cm2, BMD T-score and BMD Z-score. Osteoporosis was diagnosed according to the criteria of the International Society for Clinical Densitometry defined by a BMD T-score < 2.5 at the FN or LS (23). Data were provided on demographic characteristics, reproductive characteristics, physical activity, vitamin D, medication use such as osteoporosis medications and hormone therapy (table 1). In statistical analysis, patients and controls were compared based on BMD parameters at the femoral neck and lumbar spine. In addition, the prevalence of osteoporosis in the patient group was compared with that in the control group. Student's t test was used to compare quantitative variables and the chi-square test was used to compare categorical variables. Associations were determined by calculating odds ratios with 95% confidence intervals (CIs). Multiple regression analysis with adjusted odds ratios was used to determine independent associations.

Results

Thirty-five patients and 35 controls with mean age±standard deviation of 61.9±8.69 and 58.8±6.8 years, respectively, were studied (P = 0.67). The characteristics of the study population are presented in table 1. In univariate analysis, the values of all bone density parameters, including BMD g/cm2, BMD T-score, and Z-score of BMD at the femoral neck and lumbar spine in patients were lower than those in the control group, but the difference did not reach statistical significance (table 1).

Similarly, the prevalence of osteoporosis in patients compared with controls did not reach statistical significance (33.3% vs. 22.2%, P = 0.42). In multivariate logistic regression analysis after adjusting for all covariates such as vitamin D deficiency, general and abdominal obesity, lactation period, parity, menopause, physical activity, the association between symptomatic KOA and osteoporosis did not change and remained nonsignificant at adjusted OR = 3.14 (95% CI, 0.608-16.23, P = 0.17). Interestingly, general obesity (BMI > 30 kg/m2) was significantly associated with a reduced risk of osteoporosis in symptomatic KOA patients with an adjusted OR = 0.23 (95% CI, 0.058-0.945, P = 0.041). None of the conventional risk factors for osteoporosis such as abdominal obesity, vitamin D deficiency, physical activity, and menopause duration were associated with osteoporosis at the femoral neck or lumbar spine.

Table 1. Characteristics of study population with symptomatic knee osteoarthritis and healthy controls

Variables	Case No=35 Mean±SD	Control No=35 Mean±SD	P-values
Age, year	61.9±8.69	58.9±6.8	0.67
Age>60 years, no (%)	21 (60)	14 (40)	0.33
Duration of lactation, months	22.6±17.8	20.2±11.9	0.52
Age of menopause, years	47.6±8.9	47.6±9.3	0.90
Abdominal obesity, no (%) ₩,	32 (91.4)	31 (88.6)	0.92
Waist circumference, cm	11 ±17.6	108.2±15.7	0.46
Parity	4.14 ±2.2	l3.34±1.67	0.09
No of children (%) > 3	21 (60)	16 (45.7)	0.5
Vitamin D deficiency, no (%) #	33 (94.3)	12 (34.31	0.007
Body mass index, kg/m ^{2}	30.6±5.3	29.4±3.7	0.62
General obesity, no (%) &	18 (51.4)	16 (45.7)	0.77
Menopausal duration, years	13.4±1.6	13.0±1.4	0.28
Menopausal duration > 5 years, no(%)	27 (77.1)	24 (68.6)	0.74
Lactation period > 12 months, no (%)	25 (71.4)	24 (68.5)	0.91
Weekly physical activity >3 hours, no (%)	10 (28.5)	15 (43)	0.38
FNBMD g/cm ^{2}	0.835±217	0.862±0.23.9	0.62
LS-BMD g/cm ^{2}	1.067±0.276	1.07-1.58	0.92
FN T –score	-1.44±1.62	-1.044±1.94	0.35
FN Z- score *	-0.335±1.57	-0.188±1.92	0.73
LS T-score *	-1.099±1.89	-0.331±2.01	0.10
LS Z- score *	0.0364±1.82	0.482±2.03	0.34
FN-Osteoporosiss no (%) ¥	10 (27.7)	6 (16.6)	0.36
LS-Osteoporosis, no (%)	9 (25)	6 (16.1).	0.48
Either FN or LS Osteoporosis, no (%) ¥	12 (33.3)	8 (22.2)	0.42
Physical activity> 3 h weekly, no (%) *	10 (27.7)	15 (41.6)	0.38
Age > 60 years, no (%)	21 (58.3)	14 (38.02)	0.33

* Self-reported data

Serum 25 hydroxyvitamin D ≤ 20 ng/ ml

¥ LS (lumbar spine) and FN (Femoral neck) Osteoporosis defined as BMD T-score ≤ -2.5

₩ Abdominal obesity defined as waist circumference > 95 cm

& General obesity defined as BMI ≥ 30 kg/ m^2

Table 2. Independent association between symptomatic knee osteoarthritis and risk of osteoporosis at the femoral neck or lumbar spine after adjustment for other covariates by multiple regression`n analysis

	Adjusted odds ratio	95% (confidence interval).	P-value
Patients vs Controls	3.143	0.608-16.23	0.172
Vitamin D Deficiency vs sufficiency	0.937	0.068-12.90	0.961
Abdominal obesity Yes vs No	1.000	0.149-6.71	1.000
Obesity BMI <30 vs ≥ 30 kg/m^2	0.234	058-.945	0.041
PhysicalActivity ≤ 3 h weekly vs > 3 h weekly	1.246	0.305-5.09	0.760
Menopausal duration, years≥ 5 years vs < 5 years	1.733	0.455-6.60	0.420
Parity ≤ 3 children vs > 3 children	0.526	0.145-1.90	0.327
Lactation period ≥12 months vs < 12 months	2.003	0.552-7.26	0.291

BMI: Body mass index, kg/m ^{2}

Discussion

The results of this study showed no association between symptomatic KOA and osteoporosis in postmenopausal women. However, there was a trend toward no significantly lower values of all BMD parameters in symptomatic KOA patients compared with controls. Furthermore, the difference in osteoporosis at the femoral neck and lumbar spine was not significant (33.3% vs 22.2%). However, almost similar prevalence rates of osteoporosis were reported in two previous studies of KOA patients, 39.5% and 23%, respectively (16, 11). The relationship between BMD and KOA varies among studies (10, 12-17). The results of our study are consistent with the results of several previous studies (10, 14, 15). Bae and *et al*., (14) in a study of Korean men and women over 65 years of age found no significant differences in BMD values between men and women with and without radiographic osteoarthritis of the hands or knees (14). Similar observations were also observed in a study of vitamin D-deficient postmenopausal women with primary KOA aged 40 to 60 years (10). Furthermore, in the Baltimore Longitudinal Study, there was no association between hip BMD values and radiographic changes in KOA in either men or women (15). However, several studies have found lower BMD in KOA patients compared with controls (12, 13). In a study of 195 patients with symptomatic KOA, low BMD at the proximal femur (femoral neck, trochanter, intertrochanteric, and total hip) was positively correlated with joint space width (12). However, the participants in this study were different from ours. The mean age was higher and BMD was lower, with a K-L grade of 3 or 4 on radiographs in 73% of patients. Wen and *et al*., (13) in a study of men and women found an inverse association between KOA scores and BMD of the femoral neck and lumbar spine. Conversely, two studies found higher BMD values in patients with osteoarthritis (16, 17). In the fourth and fifth cohorts of the Korean National Health and Nutrition Examination Survey, adjusted BMD values at the femoral neck and lumbar spine were significantly higher in subjects with KOA. Among KOA patients, there is an inverse relationship between BMD and KOA severity (16). In the Chinford study population, a slight increase in BMD was observed in middle-aged women with early-onset osteoarthritis of the hands, knees, and spine (17). The inconsistent results between studies may be due not only to the characteristics of the study population, such as age, risk factors, and severity of KOA (1, 2), but also to the study design, sample size, and common coexisting conditions that are associated with KOA patients and have opposing effects on bone mass.

For example, osteoarthritis and osteoporosis share multiple risk factors, including age, vitamin D deficiency, muscle weakness, inflammation, obesity, and mechanical overload (24). Obesity and mechanical overload accelerate the progression of osteoarthritis, but may have a preventive effect on BMD loss (3, 7, 25, 26). Our study has certain limitations. The small sample size is the main limitation. With larger samples, smaller differences may be detected. Another limitation of this study may be the poor concordance between clinical criteria for ACR and symptomatic KOA. We did not perform knee radiographs

in the control group. The low specificity of the ACR criteria may have made it possible to include asymptomatic KOA in the control group and subsequently underestimate the difference in BMD. Another limitation of this study may be attributed to inaccurate self-reported data. Most postmenopausal women typically take calcium and vitamin D to prevent osteoporosis and fractures. However, we did not include patients who had received calcium or vitamin D in the three months prior to inclusion in the study. Since the collected data are self-reported, the impact of potential over- or underestimation cannot be excluded. However, the effect on the statistical analysis is expected to be minimal because the distribution of participants taking these medications in both the case and control groups is likely similar and should not significantly affect the results.

However, our study was interested in collecting data to support the results. Data regarding many factors associated with KOA and bone loss such as physical activity, obesity, age, and menopause were similar between the two groups. Therefore, the presence of changes in BMD between groups is unlikely. However, the impact of symptomatic knee OA on BMD is a long-term process and cannot be demonstrated in a cross-sectional study but must be demonstrated in a longitudinal study. In conclusion, the results of this study demonstrate no significant differences in bone mineral density (BMD) or the prevalence of osteoporosis between patients with symptomatic knee osteoarthritis (KOA) and healthy controls. The clinical relevance of these findings lies in the observed lack of association between low physical activity and osteoporosis in postmenopausal women with symptomatic knee osteoarthritis. This suggests that the potential negative effect of low physical activity on bone mass may be counterbalanced by weight gain, which could exert a protective effect on bone density. However, it is important to recognize that further longitudinal studies with larger sample sizes are required to thoroughly explore and confirm these findings.

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Conflict of interests: None declared.

Authors' contribution: Conceptualization: KN and MB, Data curation: KN, Formal analysis: MB and KN, Methodology: MB and KN, Project administration MB, Resources: KN and MB. Supervision: MB, Validation: MB and KN

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