Correlation of Femoral Cartilage Thickness and Osteoporosis in Female Patients with Knee Osteoarthritis

Diz Osteoartritli Hastalarda Femoral Kıkırdak Kalınlığı ve Osteoporoz İlişkisi

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Abstract

Objective: To evaluate the relationship between ultrasonographic femoral cartilage thickness and presence of concomitant osteoporosis in a group of female patients with knee osteoarthritis (OA).

Materials and Methods: This study included 118 women with knee OA who visited our outpatient clinic. Demographic data were collected, radiologic grading using Kellgren Lawrence (K-L) scale, ultrasonographic femoral cartilage thickness (FCT) evaluation, pain intensity evaluation, disability evaluation using OA index [Western Ontario and McMaster Universities Osteoarthritis index (WOMAC)], quality of life measurement using Short Form-36 (SF-36) and bone density measurement using dual-energy X-ray absorptiometry (DXA) were conducted for each patient.

Results: We found that 58 patients (median age: 64.5 years, range: 50-75) had osteoporosis (group 1) and 60 patients (median age: 62 years, range: 51-75) did not have osteoporosis (group 2). Group 2 had higher body mass index (BMI) in addition to lower WOMAC, SF-36 physical function, physical role limitation, pain and social function scores. The severity of osteoporosis and K-L staging were negatively correlated. The DXA femoral neck and total lumbar T-scores were higher in the advanced stages of OA. FCT had no significant correlation with age, WOMAC index and SF-36 scores. Moreover, the left knee FCT was negatively correlated with BMI.

Conclusion: Radiologic staging of OA had a negative correlation with osteoporosis but no significant correlation with the quantitative measurement of FCT using ultrasonography.

Keywords: Femoral cartilage thickness, knee osteoarthritis, osteoporosis, ultrasonography, SF-36, WOMAC

Öz

Amaç: Diz osteoartriti (OA) olan kadın hastalarda ultrasonografik femoral kıkırdak kalınlığı ve eş zamanlı osteoporoz varlığı arasında ilişki olup olmadığının araştırılmasıdır.

Gereç ve Yöntem: Çalışmaya, polikliniğe başvuran ve her iki dizinde OA bulunan 118 kadın hasta dahil edildi. Hastaların demografik verileri, radyolojik Kellgren Lawrence (K-L) evreleme, ultrasonografi ile femoral kıkırdak kalınlığı (FKK) ölçümü yapıldı. Numerik ağrı değerlendirmesi, OA indeksi [Western Ontario ve McMaster Universitesi Osteoartrit indeksi (WOMAC)], genel sağlık ölçütü ve yaşam kalitesi değerlendirmesi Kısa Form-36 (SF-36) ve kemik mineral yoğunluğu için çift enerjili X-ışını absorbsiyometrisi (DXA) yapılarak kaydedildi.

Bulgular: Yaş ortalaması 64,5 (aralık: 50-75) olan 58 hastada osteoporoz mevcut iken (grup 1), yaş ortalaması 62 (aralık: 51-75) olan 60 hastada osteoporoz yoktu (grup 2). Grup 2'de vücut kitle indeksi (VKİ) daha yüksek bulundu. K-L evreleme arttıkça osteoporoz insidansı azalma eğilimindeydi. İleri evre OA'da DXA femur boyun, lomber total T-skor ölçümleri yüksek saptandı. Osteoporoz olmayan grupta istatistiksel olarak WOMAC ağrı, tutukluk, fonksiyon ve total skorları daha yüksek, SF-36 fiziksel fonksiyon, fiziksel rol kısıtlanması, ağrı, sosyal fonksiyon skorları daha düşük saptandı. Osteoporoz varlığı ve K-L evreleme ile FKK ölçümü arasında anlamlı ilişki saptanmadı. Sol diz FKK VKİ ile negatif korelasyon göstermekteydi.

Sonuç: Radyolojik OA ve osteoporoz arasında negatif ilişki saptanmıştır. Ultrasonla FKK ölçümü ve diz OA derecesi arasında anlamlı bir ilişki gözlenmemiştir.

Anahtar kelimeler: Femoral kıkırdak kalınlığı, diz osteoartriti, osteoporoz, ultrasonografi, SF-36, WOMAC

Introduction

Osteoarthritis (OA) is a major cause of disability and is among the most frequent forms of musculoskeletal disorders. It is characterized pathologically with both focal loss of articular cartilage and marginal and central new bone formation. The knee particularly is assumed to be an important healthcare problem associated with symptoms of pain and functional disability (1).

Osteoporosis is called the "silent thief" because it steals bone without immediate consequence or attention, and it results in low bone mass and the structural deterioration of bone, ultimately leading to fragility fractures. Fractures of the spine and hip are known to be the major determinants affecting quality of life in elderly people. Antiresorptive (bisphosphanates and denosumab) and anabolic (parathormone, growth hormone) medications have been developed to prevent and treat those people at risk (2).

Though relationship between osteoporosis and OA is presumed to be completely controversial with differences in risk factors; bone mineral density (BMD), body mass index (BMI), phenotype, morbidity and mortality, they share some epidemiological profiles and in both diseases bone metabolism plays a crucial role in the pathophysiology. Several recent reviews have summarized the extensive literature on cross-sectional and prospective cohort and population-based studies that discuss the relation between OA and osteoporosis. This relation is complex, in terms of BMI, BMD, bone loss, subchondral bone changes, genetic background, fracture risk and the role of mechanical and systemic factors. Furthermore, in the literature, there is considerable heterogeneity in the way OA is defined. OA is a heterogeneous disease in terms of staging (early versus late), location (weight-bearing versus nonweight-bearing and monoarticular versus polyarticular), definition (clinical and radiographic), classification (according to concomitant inflammation or sequential involvement of cartilage, bone and connective tissue), risk factors (local or systemic) and methods of imaging [radiography, magnetic resonance imaging (MRI), ultrasonography (USG)] (3).

In the Framingham study, it was found that femoral BMD was higher in those with osteophytosis of the knee, and that BMD is not necessarily associated with joint space narrowing among women (4). In the Rotterdam study, radiographic OA was associated with high BMD and also increased rate of bone loss (5). Both of these studies have the largest sample sizes with 1,154 and 2,745 patients respectively. There are some other studies with conflicting results (6-8).

This cross-sectional study observes the relationship between radiologic or ultrasonographic knee OA and osteoporosis of the lumbar and femoral regions. Concurrently, the correlation of ultrasonographic evaluation with demographic factors and disability is also investigated.

Materials and Methods

In this cross-sectional population based study, 118 female patients were included with knee OA according to 1986 ACR criteria who attended to our outpatient clinic (9). Demographic data as age, menopause status, current osteoporosis treatment and BMIs (kg/m^2) were checked. Radiologic staging of knee OA by Kellgren Lawrence (K-L) (10), ultrasonographic femoral cartilage thickness (FCT) by 11-MHz lineer transduser (GE Healthcare, Logiq P5), pain intensity evaluation by numeric pain scale (NPS) (11), disability evaluation by osteoarthritis index [Western Ontario and McMaster Universities Osteoarthritis index (WOMAC)] (12), quality of life measurement by Short Form-36 (SF-36) (13,14) and BMD measurement by dual-energy X-ray absorptiometry (DXA) (15) were done for each patient. The patients were seperated into 2 groups with (G1) or without osteoporosis (G2).

Inclusion criteria were to be female, ages between 50-75 and OA staging of K-L between 1 to 3 for knee OA. Exclusion criteria were; to be K-L staging 4, to have had a surgical procedure, concommittant inflammatory arthritis, plegia or neuropathic disorders and using glucosamine/chondroitin sulfate supplements. Uludağ University Clinical Research Ethics Committee approval was obtained for the study with the number of 2016-7/13 (date: 12.04.2016). All subjects who met the study criteria were informed of the nature of the study and a written consent was obtained.

Ultrasonographic evaluation was done by ultrasound while the patient lied in supine position with her knees in maximum flexion. The ultrasound probe was placed on the suprapateller region in axial plan in order to view the unechoic femoral cartilage between the cortex and the suprapatellar fat. The FCT was measured at medial, intercondylar and lateral regions to calculate the average thickness (Figure 1).

DXA measurements were done by Hologic Horizon Wi S/N 201290 at the university hospital radiology unit. T-scores below -2.5 for lumber total, femur neck (FN) and femur total (FT) BMDs were accepted as osteoporosis referring to World Health Organization classification criteria. The BMD value of the discrete/crushed vertebrae corpus was subtracted from the value of total lumbar BMD for not causing a wrong decision (Figure 2).

NPS is a one-dimensional 11-point numeric scale ranges from '0' representing 'no pain' to '10' representing the pain' as bad as you can imagine'. For construct validity, the NPS was shown to be highly correlated with the visual analogue scale in patients with rheumatic and other chronic pain conditions; correlations range from 0.86 to 0.95.

WOMAC is a disability scale for OA containing 3 parts; pain (5 questions), stiffness (2 questions) and physical function (17 questions) in which Likert scale between 0-4 is used for evaluation. The scores increse as the symptoms get worse. Validity and reliability study for Turkish version of WOMAC was published previously (12).

SF-36 is a measurement tool for quality of life containing totaly 36 questions in 8 divisions; physical functioning, physical role limitation, emotional role limitation, bodily pain, social functioning, mental health, vitality and general health. Scores

are between 0-100 while high scores match with better health status. Validity and reliability study for Turkish version of SF-36 was published previously (13,14).

Statistical Analysis

The statistical analyses were done with SPSS version 21.0. Shapiro-Wilk test was used to test the normality of variables. Descriptive statistics were explained as mean ± standard deviation or median (maximum-minimum) for normal distribution or not respectively. Pearson's chi-squared and Yates corrected chi-squared tests were used for descriptive statistics for cathegorical data of independent groups. One-Way ANOVA was used for double comparison of multivariate data. Kruskal-Wallis test was used for the comparison of multivariate data which were not normally distributed. Correlations between the normally distributed variables were calculated by Pearson correlation test. Spearman correlation test was used for the variables which were not normally distributed. The level of significance for all tests was taken as α=0.05.

Results

Totally 118 patients between the ages of 50-75 were included in the study. Fifty-eight patients with median age of 64.5 (50-75) had osteoporosis (group 1) and 60 patients with the median age of 62 (51-75) did not have (group 2). Thirty-five patients in the osteoporotic group were taking antiresorptive medication (29 of them were taking bisphosphonates and 6 of them were taking denosumab medication). Remaining 23 patients in group 2 were only taking vitamin pills irregularly. Patients in group 2 had higher BMI (p=0.000), worst WOMAC scores (pain, stiffness, function, total) (p=0.003, p=0.019, p=0.000, p=0.001 respectively) and lower SF-36 scores (physical function, physical role limitation, pain, social function) (p=0.008, p=0.017, p=0.006 respectively) baseline. FCT was not statistically different in both of the groups (Table 1).

Right knee K-L OA staging was as follows: 34 knees stage 1, 50 knees stage 2, 34 knees stage 3. Left knee K-L staging was as follows: 38 knees stage 1, 49 knees stage 2 and 31 knees stage 3. K-L staging of
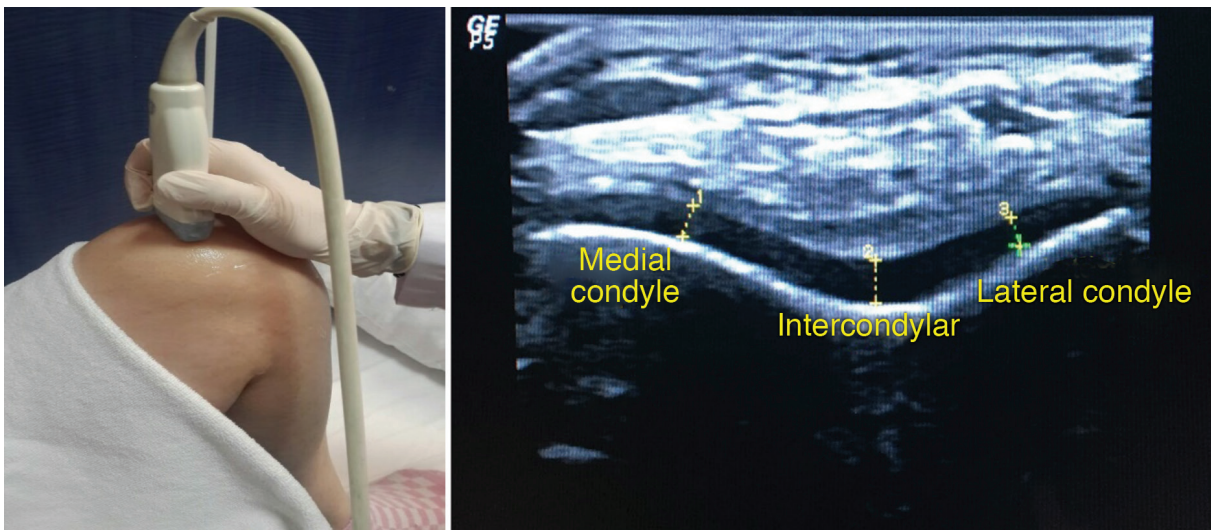
Figure 1. Positioning the ultrasonographic probe in axial plan and imaging the cartilage in 3 points

Figure 2. Bone mineral density and T-score measurement by dual-energy X-ray absorptiometry

the knees were in reverse relationship with osteoporosis according to T-scores. Osteoporosis decreased as the K-L stage increased. Femoral neck and lumbar total T-scores of BMD measurements were higher in the advanced stages of OA at both right and left knees (p=0.015 for FN and p=0.003 for LT T-scores of right knee, p=0.045 and p=0.012 for FN and LT T-scores of left knee). BMI had positive correlation with radiologic K-L grading (p<0.001). (Table 2).

In double comparisons of the variables; the right knees having grade 3 OA had higher FN T-scores when compared to knees with grade 2 OA (p=0.014). Similarly knees with grade 3 OA had better LT T-scores when compared to knees with grade 1 and 2 OA (p=0.05). In the left knees; patients with grade 3 OA had higher FN T-scores when compared to patients with grade 1 OA (p=0.041). Invariably grade 3 OA had higher LT T-scores when compared to grade 1 OA (p=0.003). Other double comparisons were statistically insignificant.

The correlation of FCT with demographic data, disability and general health variables put forth only BMI for consideration

which was negatively correlated to FCT at the left knee (p=0.041, r=-0.189) (Table 3).

Discussion

In this cross-sectional observational study we determined that 1) knee OA patients without osteoporosis had worse scores in quality of life and disability when compared to the group of patients with osteoporosis in which higher BMI maybe the key factor, 2) there was a negative relationship between osteoporosis intensity and K-L staging of OA, 3) there was no significant correlation between FCT of the osteoarthritic knees and any other variables except BMI. 4) High BMI was in negative corelation with osteoporosis and FCT of the left knee.

The population-based Chingford study revealed the positive correlation between generalised OA and BMD in 1994 (16). In the Framingham study it was found that femoral BMD was higher in the group of female patients with knee OA with osteophytosis when compared to the group without

Table 1. Demographic variables and basic evaluations of the patients with knee OA according to the existence of concomittant osteoporosis

	Group 1 with OP (n=58) Median (min-max)/mean ± SD	Group 2 without OP (n=60) Median (min-max)/mean ± SD	p
Age	64.5 (50-75)	62 (51-75)	0.516
Menopause age	46.67±5.42	45.53±6.00	0.282
BMI (kg/m²)	27.51 (20-40)	31.22 (23-42)	0.000
Right knee medial FCT (mm)	1.46±0.50	1.39±0.39	0.421
Right knee intercondylar FCT (mm)	1.60 (0.33-2.99)	1.73 (0.89-3.70)	0.228
Right knee lateral FCT (mm)	1.56 (0.22-2.74)	1.56 (0.80-2.92)	0.454
Right knee average FCT (mm)	1.54±0.44	1.61±0.38	0.370
Left knee medial FCT (mm)	1.44±0.49	1.40±0.35	0.667
Left knee intercondylar FCT (mm)	1.73±0.51	1.73±0.41	0.874
Left knee lateral FCT (mm)	1.39±0.44	1.47±0.42	0.319
Left knee average FCT (mm)	1.52±0.39	1.53±0.30	0.849
WOMAC-pain	2 (0-8)	3.5 (0.5-7.5)	0.003
WOMAC-stiffness	2.5 (0-10)	3.75 (0-10)	0.019
WOMAC-function	2.13 (0-6.91)	3.45 (0.44-6.91)	0.000
WOMAC-total	6.35 (0.5-23.38)	10.49 (0.94-22.37)	0.001
SF-36 physical function	55.0 (10-100)	42.5 (0-95)	0.008
SF-36 physical role limitation	100 (0-100)	0 (0-100)	0.017
SF-36 pain	51.0 (22-100)	41.0 (2-84)	0.006
SF-36 general health	61.0 (15-82)	60 (5-86)	0.326
SF-36 energy	45.0 (0-95)	40.0 (0-90)	0.320
SF-36 social function	87 (25-100)	68.5 (25-100)	0.040
SF-36 emotional role limitation	100 (0-100)	100 (0-100)	0.191
SF-36 mental health	72.0 (20-180)	60.0 (14-100)	0.710

OA: Osteoarthritis, OP: Osteoporosis, BMI: Body mass index, FCT: Femoral cartilage thickness, SF-36: Short Form-36, WOMAC: Western Ontario and McMaster Üniversity Osteoarthritis index, min: Minimum, max: Maximum, SD: Standard deviation

osteophytosis (4). In 2 of the osteoporotic fracture studies it was found that patients with coxarthrosis had higher BMD but fracture risk has remained the same (17,18). This last result was also supported by Rotterdam study in which it was come to a conclusion that vertebral and nonvertebral fracture risk was higher in the patients with knee OA, independent of the BMD variables (5). High BMI, genetic factors, subchondral sclerozis and sitokines like IGF-1 and TGF-B are assumed to be the risk factors for OA, though the relationship with the BMD still remains partly undefined (19). In our study it was found that later stages of OA was positively correlated with higher BMD, supporting the Chingford and Framingham studies (4,16). The hypothesis of negative correlation between OA and osteoporosis was corroborated.

Another study revealed that later stages of knee OA was together with lower proximal femoral BMD scores ipsilaterally because of not using the extremity to avoid pain. The lomber BMD was not influenced by this result (20). There is positive and strong evidence that osteophytosis may be with or cause higher BMD (21). High BMI (obesity) is a very important risk factor for OA while it is a relative protective factor for osteoporosis (22,23). Bone mineral loss slows in the patients with excessive fat tissue producing estrogen which is responsible for the release of IGF-1 and TGF-B from the osteblasts and by mitogenic response to leptin and hyperinsulinemia (24,25). Obesity may cause degenerative processes like OA which may be also related to high adipokine levels and inflammation (26). Because it is also a disability determinant and pain generator by mechanic and metabolic reasons, Osteoarthritis Research Society International recommend to get weight loss by at least 5% in 20 weeks time (27).

In the literature, there is a moderate-strong correlation between reliability of MRI and USG for evaluation of the FCT. Middle

Table 2. K-L staging of the right and left knees and their relation with the BMD T-scores

	FN (T-score) Mean ± SD	LT (T-score) Mean ± SD	FT (T-score) Mean ± SD	BMI (kg/m²) Mean ± SD
Right knee K-L stage 1 (n=34)	-1.40±1.06	-2.04±1.10	-0.87±1.10	27.79±17.41
Right knee K-L stage 2 (n=50)	-1.50±0.94	-2.03±0.94	-1.03±0.95	29.29±18.45
Right knee K-L stage 3 (n=34)	-0.80±1.47	-1.22±1.39	-0.48±1.11	31.92±20.72
p	0.015	0.003	0.066	0.000
Left knee K-L stage 1 (n=38)	-1.47±1.17	-2.5 (-3.8-0.1)	-0.93±1.13	27.75±18.41
Left knee K-L stage 2 (n=49)	-1.43±0.80	-2.1 (-3.1-0.9)	-0.94±0.87	29.28±17.61
Left knee K-L stage 3 (n=31)	-0.84±1.45	-1.3 (-4.5-2.0)	0.54±1.12	31.91±22.30
p	0.045	0.012	0.206	0.001

K-L: Kellgren Lawrence, FN: Femur neck, LT: Lomber total, FT: Femur total, SD: Standard deviation, BMI: Body mass index

Table 3. Correlation of FCT with demographic variables, quality of life and disability scores

	Right knee FCT		Left knee FCT	
	r	p	r	p
Age	-0.096	0.301	-0.052	0.173
BMI	-0.158	0.088	-0.189	0.041
NPS	0.064	0.494	-0.060	0.518
WOMAC-pain	0.100	0.281	0.083	0.374
WOMAC-stiffness	0.001	0.992	0.013	0.893
WOMAC-function	0.058	0.531	0.034	0.716
WOMAC-total	0.060	0.519	0.044	0.637
SF-36 physical function	-0.070	0.453	-0.020	0.828
SF-36 physical role limitation	0.054	0.560	0.022	0.811
SF-36 pain	-0.020	0.832	0.001	0.992
SF-36 general health	-0.014	0.882	0.079	0.393
SF-36 energy	0.052	0.574	0.102	0.272
SF-36 social function	-0.007	0.942	-0.021	0.818
SF-36 emotional role limitation	0.042	0.655	0.063	0.499
SF-36 mental health	0.136	0.141	0.161	0.081

FCT: Femoral cartilage thickness, SF-36: Short Form-36, WOMAC: Western Ontario and McMaster University Osteoarthritis index, BMI: Body mass index, r: Correlation coefficient, NPS: Numeric pain scale

intercondyller notch seems to be the best anatomic place to measure (28,29). In this study USG is preferred for evaluation because of its reliability, repeatability and cheapness.

Dequeker et al. (24) claimed that excessively high subchondral bone density may cause progressive chondrocyte disfunction in the early stages of cartilage destruction. Increase of the peak mechanical stress at the cartilage of the weight bearing bone with high BMD plays the major role in OA (30). Some other studies have contradictory results in which low BMD means high bone remodelization, with similar accelerating effect on cartilage turnover and inadequate restoration (3,31,32).

These literature knowledge reveals the conflicting and complex relationship between these 2 diseases with several contributing factors in the intersecting etiology such as metabolic, mechanical, genetic or endocrinologic. Low BMI is a risk factor for osteoporosis while high BMI is a risk factor for OA progression as also explained in our study. There was not an association between ultrasonographic FCT and osteoporosis in our study similar to another submitted study by Çarlı et al. (33).

Study Limitations

Limitations of the study were; patients having antiresorptive medication were not excluded, and the sample size is relatively low according to these type of observational studies. Bisphosphonates are antiresorptive agents used for treating osteoporosis and have inhibition effect on osteoklasts. Because it's thought that antiresorptive medication decreases both bone and cartilage turnover, it's reasonable to think that supression of the subchondral bone remodeling may cause a common advantage by delaying the subchondral bone sclerozis and osteophyte formation in OA and may have changed the long term clinic progress (34-39).

Conclusion

Later stages of OA may be positively correlated with high BMD but this is still a question in dispute that if it is a cause or a result? As a conclusion, high BMI may lead to OA progression and disability but has protective effect for osteoporosis. There is also a reason to think that, DXA BMD measurements may be false negative in later stages of OA, because of osteophytosis and subchondral bone sclerozis. There is a need for studies evaluating ultrasonographic FCT with larger sample sizes and may be combined with laboratory detection of cartilage destruction products and its relationship with osteoporosis medication.

Ethics

Ethics Committee Approval: Uludağ University Clinical Research Ethics Committee approval was obtained for the study with the number of 2016-7/13 (date: 12.04.2016).

Informed Consent: All subjects who met the study criteria were informed of the nature of the study and a written consent was obtained.

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Authorship Contributions

Surgical and Medical Practices: G.A.Ö., Concept: A.A., G.A.Ö., Design: A.A., G.A.Ö., Data Collection or Processing: A.A., G.A.Ö., Analysis or Interpretation: A.A., G.A.Ö., Literature Search: A.A., G.A.Ö., Writing: A.A.

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