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Ultrasonographic Characteristics of Femoral Trochlear Cartilage in Patients with Knee Osteoarthritis

ORIGINAL INVESTIGATION

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ABSTRACT

Objective: We aimed to measure the femoral trochlear cartilage thickness using musculoskeletal ultrasound (US) and examine the effects of cartilage characteristics on the quality of life and functional status in postmenopausal women diagnosed with knee osteoarthritis (OA).

Materials and Methods: We examined 42 female patients and included a control group comprising 21 healthy women with similar age. Cartilage thickness, clarity, and subchondral bone calcification were evaluated using US with 5–13-MHz linear probe; pain and functional status were evaluated using the Western Ontario and McMaster Universities (WOMAC) OA index; and the quality of life was evaluated using Short Form-36 (SF-36).

Results: A positive correlation was observed between measurements of 25-OH vitamin D levels and left intercondylar region, left lateral condyle, and right intercondylar area (r=0.416, p=0.006; r=0.421, p=0.001; and r=0.398, p=0.031, respectively). The quality of cartilage clarity was better in the patient group than in the control group for both knees (p<0.05). Cartilage clarity scores of the patients were positively correlated to the WOMAC total score and negatively correlated to the SF-36 total scores (left knee, r=0.159, p=0.314; right knee, r=0.261, p=0.096 and left knee, r=−0.263, p=0.093; right knee, r=−0.312, p=0.044, respectively).

Conclusion: Compared with cartilage thickness, cartilage clarity appears to be a very successful parameter in reflecting the patient's quality of life and functional status.

Keywords: Femoral cartilage, knee osteoarthritis, ultrasonography

INTRODUCTION

Osteoarthritis (OA) is a degenerative disease that is particularly common in load-bearing joints such as the hip and knee and is characterized by joint cartilage damage, joint space narrowing, subchondral sclerosis, and osteophyte (1).

There are some local (previous damage, malalignment, and muscle weakness) and systemic (age, female gender, race, genetic predisposition, and obesity) risk factors that trigger OA (2). Furthermore, although results are inconsistent, the deficiency of certain vitamins, such as A, D, E, and K, and other trace elements could increase the risk for OA (3-7).

In OA, progressive thinning of the joint cartilage occurs; therefore, the evaluation of cartilage thickness is unquestionably important to assess and monitor the severity of the disease. When considering the major efforts in developing new medical and surgical treatments for OA, the evaluation of articular cartilage becomes very important (8, 9). Therefore, ultrasound (US) is a valid and reliable method for evaluating femoral trochlear cartilage and is used in an appropriate manner (10-13). The various advantages of sonography (non-invasive, widely used, reproducible, does not include ionizing radiation, dynamic imaging, and comparison) make its immediate application by physicians and ready acceptance by patients possible. Likewise, it is most commonly used for monitoring the joint disease of OA (9-11, 13, 14).

This study aimed to investigate the effects of cartilage thickness and 25-OH (hydroxyl) vitamin D levels on the functional status and quality of life in postmenopausal women who were diagnosed with knee OA using musculoskeletal US for measuring the femoral trochlear cartilage thickness.

MATERIALS and METHODS

We enrolled 42 postmenopausal women who were admitted to our clinic between June and December 2014 with knee pain and were diagnosed with OA according to the American College of Rheumatology (ACR) criteria (1) and

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who fulfilled the inclusion criteria and accepted to participate in the study. A control group comprising 21 healthy female volunteers was also enrolled.

The study was approved by the local Ethics Committee. Patients participating in the study were informed about the aim of the study, including oral and written information regarding the procedure. Patients who voluntarily signed the informed consent form were enrolled.

The inclusion criteria were knees with a diagnosis of primary OA, according to the ACR criteria; women aged 40–75 years; and radiological findings of grade 2-3, according to the criteria of the K-L grade system.

The exclusion criteria included knee OA secondary to inflammatory joint disease and patients diagnosed with secondary OA; those who had intra-articular corticosteroid and/or hyaluronic acid injections in the last 3 months; those with history of intramuscular or oral corticosteroid use in the last 3 months; trauma associated with the knee; operation; history of arthroscopic procedure; knee pain related to another cause (ligament injury, grade 3-4 meniscopathy, osteonecrosis, chondromalacia patella, etc.); flexion and/or extension limitation/contracture of the knee that would prevent US evaluation; and the use of A, D, E, K, Zn, or antioxidant.

Patients' history, physical examination, and results of the necessary laboratory tests were obtained. Individuals' age, sex, BMI (kg/m^2), exercise (at least 30–60 min of walk in a week the last 3 months), and smoking habit were recorded. Complete blood count, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), alkaline phosphatase (ALP), calcium and phosphorus, 25-hydroxy vitamin D (25-OH vitamin D), and parathyroid hormone (PTH) levels were measured. Patients' standard anteroposterior and lateral standing radiographs were obtained. Radiologic grading was done according to the K-L grading system. Our study included patients who were classified as grade 2 and 3 according to this classification.

Ultrasonographic assessment

Trochlear femoral cartilage thickness was measured as mentioned below using a 5–13-MHz linear transducer US device (LOGIQ P5; General Electric, New York, NY).

Femoral trochlear cartilage thicknesses of the subjects were assessed in the supine position with maximum flexion of the knees. The transducer was placed in the axial position at the suprapatellar region. Cartilage thickness was defined as the distance between the thin hyperechoic line that is between the synovial space and cartilage interface and the hyperechoic line that is between the line cartilage and bone [14]. Femoral trochlear cartilage thickness has a diurnal rhythm in healthy subjects [15]. Hence, measurements of femoral trochlear cartilage thickness were performed at certain time intervals at 2.00–5.00 pm. Measurements were obtained from the left intercondylar area (LIA), left lateral condyle (LLC), left medial condyle, right intercondylar area (RIA), right lateral condyle, and right medial condyle (Figure 1). Furthermore, ultrasonographic parameters included the presence of osteophytes (no=0, yes=1), cartilage calcification (no=0, I=1), and subchondral bone irregulations (none=0, I=1). Cartilage clarity was defined as how well the cartilage borders could be distinguished from the overlying intra-articular soft tissues using the following scale: 1, excellent; 2, good; 3, poor; and 4, worst.

Figure 1. Bilateral femoral trochlear ultrasound image showing the cartilage measurements of the left intercondylar region (LIR), left lateral condyle (LLC), left medial condyle (LMC), right intercondylar region (RICR), right lateral condyle (RLC), and right medial condyle (RMC)

Subjects were examined by a trained ultrasonographer with 4 years of experience, after which examinations were repeated by another trained ultrasonographer with 2 year of experience; both clinicians had a rheumatology background. Interobserver agreement was performed for 30 patients.

Scales used in the clinical evaluation:

Pain and the functional status of the subjects were evaluated with Western Ontario and McMaster Universities (WOMAC) OA index, and the quality of life was evaluated using the Short Form-36 (SF-36) index.

WOMAC OA index of hip and/or knee OA is a health status questionnaire that assesses the disability associated with OA [16]. It includes a 24-point scale that examines three dimensions: pain, stiffness, and physical function. SF-36 is the most commonly used scale in assessing the quality of life, health, and physical and mental aspects and it comprises 36 items and eight subscales. Ratings ranged from 0 to 100, with 100 points being the best health status and 0 indicating a health status score that was the worst. The first of four subscale scores including physical health score, the mental health score the last four subscale scores were calculated. In this manner, the physical and mental quality of life scores were obtained (17, 18).

Statistical analysis

The Statistical Package for the Social Sciences software program was used for statistical analysis (version 20.0, SPSS Armonk, NY: IBM Corp.). Quantitative variables (clinical, laboratory, and US parameters) were indicated as mean±standard deviation (SD). The Mann–Whitney U test was used to evaluate the continuous data from a single analysis of variance between groups. Spearman's rank correlation coefficients were calculated to determine the relationship between these variables. Unweighted kappa statistics were used to calculate interobserver agreements for cartilage thickness, cartilage clarity, for the presence of osteophytes, cartilage calcification, and subchondral bone irregulations. The statistical significance level of calculation was considered to be a p value of <0.05.

RESULTS

The study included 63 people, 42 female patients diagnosed with knee OA and 21 healthy female without knee pain. There was no statistically significant difference between both groups in terms of age, BMI, smoking, and exercise ($p>0.05$). The laboratory evaluation showed no significant difference between both groups in terms

Table 1. Clinical and laboratory parameters of the patient and control groups

	Patient group (n=42)	Control group (n=21)	p
Age (years)	56.86±5.23	56.57±4.61	0.751
BMI (kg/m²)	30.91±5.62	27.98±5.01	0.096
Smoking (%)	20.4	31,8	0.918
Exercises (%)	15.9	27.2	0.367
Radiological grade	2.41±0.58	NE	NE
WOMAC			
Pain score	12.95±3.43	NE	NE
Stiffness score	5.50±1.37	NE	NE
Physical function score	46.82±9.99	NE	NE
Total score	65.57±13.61	NE	NE
SF-36			
MHS	51.41±19.20	NE	NE
PHS	56.48±19.15	NE	NE
Total Score	56.36± 20.04	NE	NE
Calcium (mg/dL)	9.10±1.45	9.35±0.53	0.545
Phosphorus (mg/dL)	3.78±0.56	3.505± 0.52	0.092
ALP (U/L)	79.8±17.26	69.52±19.38	0.063
PTH (pg/mL)	48.35±27.63	36.88±19.60	0.051
25-OH D Vit (ng/mL)	14.74±8.29	15.68±5.21	0.107
CRP (mg/L)	5.18±2.78	5.26±3.25	0.664

25-OH D Vit: 25 hydroxi vitamin D; ALP: Alkaline phosphatase; BMI: Body mass index; BMD: Body mass index; CRP: C-reactive protein; MHS: Mental health score; NE: Not evaluated; PHS: Physical health score; PTH: Parathyroid hormone; SF-36: Short form 36; WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index

of calcium, phosphorus, ALP, PTH, 25-OH vitamin D, and CRP levels (p>0.05; Table 1). The mean and SD of the WOMAC total score of patients with knee OA were 65.57±13.613. The mean and SD of the SF-36 total score was 56.36±20.048 (Table 1).

When we examined the femoral trochlear cartilage thickness measurements in the patient group, the measurements of the RIA and LIA were calculated to be 0.2111±0.0661 cm and 0.2075±0.0598, respectively, and were found to be significantly higher than those in the control group (p=0.011; Table 2). There was no significant difference among the measurements taken from other regions (p>0.05; Table 2). The average cartilage thicknesses of the patient and control groups are shown in the Figure 2. The mean cartilage thickness of the control group (n=21) was found to be 0.18±0.04 cm, and when compared with the patient group (n=42), there was no statistically significant difference in terms of average cartilage thickness (p=0.227; Figure 3). A total of 66.6% of patients (n=28) had grade 2 OA and 33.4% (n=14) had grade 3 OA. The average cartilage thickness of grade 2 OA (n=28) and grade 3 OA (n=14) patients was 0.19±0.03 cm, and there was no statistically significant difference in terms of the mean cartilage thickness between the two radiological grades (p>0.05).

Table 2. Ultrasonographic features of the patient and control groups

	Patient group	Control group	p
Thickness of the femoral trochlear cartilage (cm)			
Right			
Medial	0.176±0.052	0.1867±0.033	0.503
Intercondiler	0.211±0.066	0.1757±0.035	0.011
Lateral	0.197±0.040	0.1905±0.034	0.668
Left			
Medial	0.177±0.055	0.190±0.042	0.353
Intercondiler	0.207±0.059	0.172±0.040	0.011
Lateral	0.190±0.040	0.185±0.043	0.331
Cartilage clarity			
Right	2.48±0.74	1.81±0.87	0.002
Left	2.52±0.77	1.71±0.64	0.001
Osteophyte			
Right	0.181±0.390	0.00±0.000	0.038
Left	0.181±0.390	0.00±0.000	0.038
Calcification			
Right	0.00±0.000	0.00±0.000	1.000
Left	0.00±0.000	0.00±0.000	1.000
Subcondral bone irregularity			
Right	0.93±0.255	0.86±0.436	0.050
Left	0.95±0.211	0.76±0.359	0.171

The cartilage clarity for both knees, another parameter evaluated by US, had a better quality in the control group (p<0.05; Table 2). There was no statistically significant difference in terms of the cartilage clarity of patients, according to the radiographic grading (p>0.05).

In terms of other parameters that were evaluated by US, osteophytes were not found only in the control group and calcification was not observed in both groups. When we evaluated the irregularity of the subchondral bone, we noted that their presence were prominent in the right knee and in the control group (p=0.05), and there was no difference between both groups in the left knee (p=0.171; Table 2).

Comparison of clinical and laboratory parameters of the US measurement of the groups:

There was a statistically significant but positive correlation between 25-OH vitamin D levels and cartilage measurements of LIA, LLC, RIA (r=0.416, p=0.006; r=0.421, p=0.001; r=0.398, p=0.031, respectively), but the measurements from other regions did not show any significant correlation (p>0.05). No association between 25-OH vitamin D levels and radiographic grade, total WOMAC, and SF-36 scores was found (p>0.05).

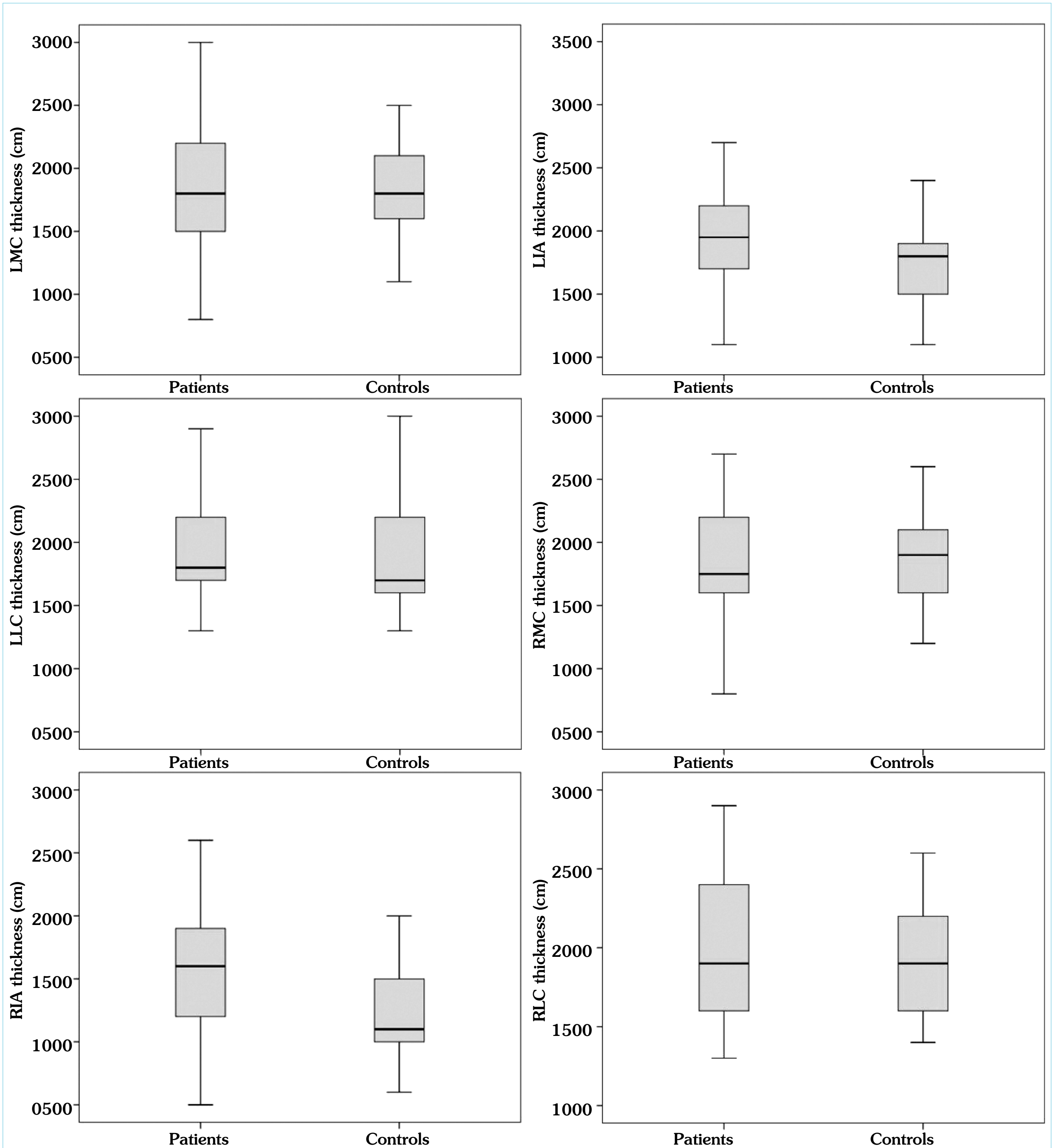

Figure 2. **The average cartilage thickness of all measurements in the patient and control groups**

When evaluating other parameters that would affect the cartilage thickness, a statistically significant negative correlation was found only between age and cartilage measurements of LLC (r=−0.308, p=0.047). A positive correlation was found only between BMI and cartilage measurements of RIA (r=0.650, p=0.001).

Comparison of cartilage clarity with WOMAC and SF-36 total scores

When classifying the cartilage clarity in terms of quality into four classes, the findings in the patient and control groups were as follows: best quality %2/38, good quality %55/42, medium quality %24/15, bad quality %19/5 (Figure 4). A positive correlation that was not statistically significant was found between WOMAC

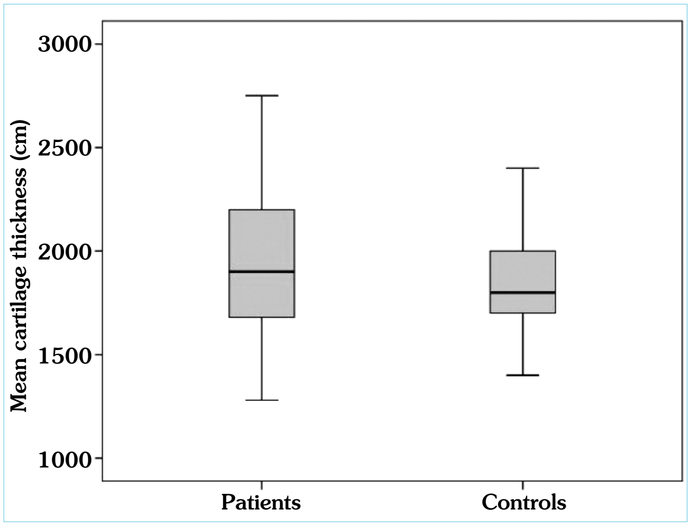

Figure 3. The mean cartilage thickness of the patient and control groups

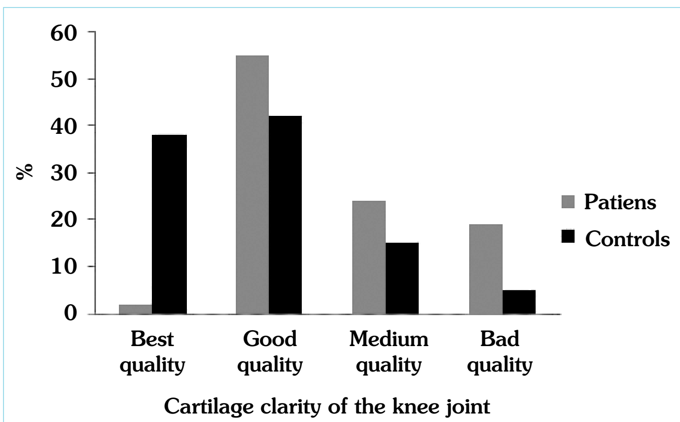

Figure 4. Classifying the femoral cartilage clarity of the patient and control groups

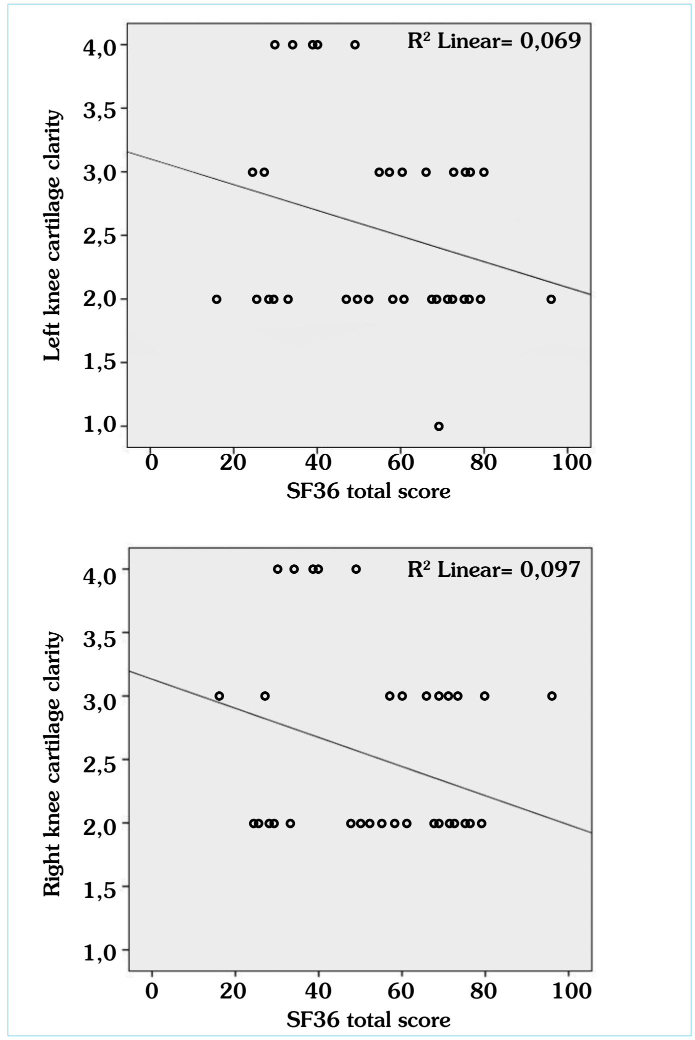

Figure 5. Relationship between patients' SF-36 scores and cartilage clarity

total scores and cartilage clarity (left knee, r=0.159, p=0.314; right knee, r=0.261, p=0.096). Meanwhile a negative correlation was found between SF-36 scores and cartilage clarity (left knee, r=−0.263, p=0.093; right knee, r=−0.312, p=0.044; Figure 5).

Interobserver reliability

The extents of interobserver agreement were 88%, 81%, 90%, 91%, and 87% for cartilage thickness, cartilage clarity, presence of osteophytes, cartilage calcification, subchondral bone irregulations, respectively, with κ values of 0.75, 0.74, 0.75, 0.77, and 0.73, respectively.

DISCUSSION

On US, normal hyaline articular cartilage is observed as a homogeneously anechoic or hypoechoic band seen in the form of a thin single layer. Although the association between aging and cartilage thickness has been investigated in several studies, a clear relationship between these two parameters remains to be established in the literature. In our study, when investigating the association between the groups of patients and cartilage thickness, a statistically significant negative correlation was found only in the cartilage measurements of LIA (r=−0.308, p=0.047). In a multicenter study conducted by Özçakar et al. (19), which included 1544 healthy volunteers with BMI of <30 kg/m^2 and aged 20–45 years, a negative correlation was found between women's femoral trochlear cartilage thickness of both knees and age in measurements performed in all regions similar with similar manners to our study. Our patient population is relatively old, and at least grade 2 OA changes in cartilage thickness are more likely to be observed. According to the study results, the loss in cartilage thickness in the premenopausal period continues to relatively decrease in postmenopausal women with OA.

In a study conducted by Cao et al. (20), which included 163 randomly selected people with a mean age of 63 years, a negative correlation was found between BMI, skeletal and total body fat, and cartilage thickness. Moreover, in the study conducted by Özçakar et al. (19), no correlation between BMI and cartilage measurements was established. In our study, the mean BMI was 30.91±5.629 kg/m^2 in patients with knee OA. However, in our study while evaluating the association between cartilage thickness and BMI, a statistically significant but positive correlation between BMI was found only with cartilage measurements of LIA, while the mean cartilage thickness and BMI did not reveal any statistically significant relationship. This is partly consistent with the literature. The investigation of the correlation between cartilage thickness and BMI may play an important role in demonstrating proving this hypothesis.

With respect to the effects of smoking on the femoral cartilage, smoking may reduce the risk for knee OA by affecting the chondrocyte metabolism of articular chondrocytes via non-nicotine on collagen synthesis activity and glycosaminoglycan upregulation (21). Therefore, smoke is a non-modifiable risk factor; however, more studies are required to understand the net effect on the non-joint cartilage. In a study conducted in 2014 by Özçakar et al. (19), a positive correlation was observed between cartilage thicknesses and smoking in women (statistically significant for just the right intercondylar space and right lateral condyle). In our study, no correlation was detected between smoking and cartilage thickness. These results might be related to the small number of patients who smoked.

In cases related to exercise, such as paraplegia and postoperative immobilization, consisting of reduced load, there is strong evidence to indicate cartilage atrophy (22). Özçakar et al. (19) revealed that there was no statistically significant difference between the femoral cartilage thickness and exercise, which is consistent with our study. The increased load does not appear to be associated with an increased mean cartilage thickness both in sedentary subjects and high-level athletes (23, 24). The lack of a higher cartilage thickness in women who regularly exercise in our study can explain this situation. One of the major shortcomings of the studies on this subject is the lack of the investigation regarding the effects of the type of exercise on cartilage thickness and clarity. This topic may be a subject for future research.

Hosseininia et al. (25) detected an increase in cartilage thickness that was caused by weakness in the connective collagen in patients with OA at an early stage because of the increase in the volume of water in their cartilage. In our study, we found no correlation between cartilage thickness and radiological stage. However, it appears that there is a slight but not statistically significant increase difference in the cartilage thickness of the patient group compared with the control group. This increase at a relatively early stage (stage 2 OA) can be associated to many of our patients.

The effect of serum 25-OH vitamin D levels on cartilage metabolism is a popular research topic that has emerged in the recent years. However, there are few studies regarding cartilage thickness. The benefits of vitamin D on bone health are related to the importance of systemic and local bone changes in OA, and some epidemiological studies are linked to the effects on OA progression (5).

Regarding vitamin D effects on cartilage thickness, study results are usually associated with an increased cartilage thickness in patients with OA whose serum 25-OH vitamin D levels are high (knee OA and temporomandibular joint OA) (26-28). In the present study, we found statistically significant but positive correlations between 25-OH vitamin D levels and cartilage measurements of LIA, LLC, and RIA ($r=0.416$, $p=0.006$) but did not observe any significant correlation with the measurements of other regions ($p>0.05$). These results appear to be consistent with those of the literature, and the low 25-OH vitamin D levels adversely affect the femoral cartilage thickness. Further studies are required to understand the clinical significance of cartilage thickness of knees and whether vitamin D supplementation can reverse cartilage thinning in patients with OA.

The basic features that make our study strong and original include a fairly comprehensive US assessment of the articular cartilage, not just stick to the articular cartilage measurements. In the assessment made using US, besides the articular cartilage thickness, articular cartilage clarity, subchondral bone irregularity, and osteophyte formation were also evaluated. According to the information obtained from the literature, this is the first study to investigate the association between cartilage clarity, assessed using US, and clinical, radiographic, and quality of life measurements. An important result of our study is the positive correlation between patients' WOMAC total scores and cartilage clarity (left knee, $r=0.159$, $p=0.314$; right knee, $r=0.261$, $p=0.096$) and the negative correlation between SF-36 scores and cartilage clarity (left knee, $r=-0.263$, $p=0.093$; right knee, $r=-0.312$, $p=0.044$). One of the secondary results of our study is that cartilage thickness is more affected by serum 25-OH vitamin D levels rather than by OA progression.

The most important outcome from these findings is that in patients with knee OA, the deterioration of cartilage clarity is initiated in early stages. Considering other studies in the literature, the reduction in cartilage thickness occurs before OA (such as premenopausal) together with aging, the measurement of postmenopausal cartilage thickness is in correlation with radiographic grade. Therefore, the evaluation of cartilage thickness and clarity for monitoring the disease severity appears to be pointless. Regardless of these findings in our study, cartilage clarity has been shown to be highly successful in reflecting the patient's quality of life and functional status compared with cartilage thickness parameters.

CONCLUSION

As a result, we could state that better the cartilage clarity is in patients with knee OA, better is the quality of life and functional status. However, this result needs to be supported by additional studies because it is the first study in this regard.

Although the small population size is an important limitation of this cross-sectional study, the results are still worth discussing. Conversely, the measurement of cartilage thickness instead of volume or technical difficulties regarding the sonographic evaluation of knee cartilage and the measurement of 25-OH vitamin D levels just once, ignoring the seasonal changes and half-life of 25-OH vitamin D level and may be among other limitations. No significant difference was found among patients with grade 2 and 3 OA in terms of both cartilage clarity and thickness.

Ethics Committee Approval: Ethics committee approval was received for this study from local ethics committee.

Informed Consent: Informed consent was obtained from patients who participated in this study.

Peer-review: Externally peer-reviewed.

Authors' Contributions: Conceived and designed the experiments or case: HH, NK, İT. Performed the experiments or case: NK, HH. Analyzed the data: HH. Wrote the paper: NK, HH, İT. All authors have read and approved the final manuscript.

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