Ultrasonographic Evaluation of Femoral Cartilage Thickness in Patients with Rheumatoid Arthritis

Romatoid Artritli Hastalarda Femoral Kıkırdak Kalınlıklarının Ultrasonografik Değerlendirilmesi

Femoral Cartilage Thickness in Patients with Rheumatoid Arthritis

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Özet

Amaç: Bu çalışmanın amacı romatoid artritli (RA) hastalarda distal femoral kıkırdak kalınlıklarında oluşabilecek değişiklikleri ultrason ile değerlendirmektir. Gereç ve Yöntem: Çalışmaya 40 RA'lı hasta ile aynı yaş grubunda 40 sağlıklı kontrol alındı. Her iki grupta ultrason ile katılımcıların distal femoral kıkırdak kalınlıkları ölçüldü. Mobiliteyi değerlendirmek için katılımcılara sandalyede kalkma testi ve 10 metre yürüme testleri uygulandı. Sağlık Değerlendirme Anketi ile hastaların yaşam kaliteleri, DAS-28 skoru ile hastalık aktiviteleri değerlendirildi. Bulgular: Romatoid artritli hastalarda kontrol grubu ile karşılaştırıldığında medial femoral kondiler kıkırdakların bilateral ince olduğu saptandı (p<0.05). İnterkondiler alan ve lateral femoral kondiler kıkırdak kalınlıklarında ise gruplar arasında anlamlı fark saptanmadı. Sandalyede kalkma ve 10 metre yürüme testlerinde RA'lı hastaların belirgin şekilde düşük performans sergiledikleri görüldü (sırasıyla p=0.000, p=0,001). RA'lı hastaların fiziksel aktivite düzeyleri de kontrol grubuna göre düşük bulundu (p=0.002). Kıkırdak kalınlıkları ile hastaların karakteristik özellikleri ve laboratuar parametreleri arasında ilişki saptanmadı. Tartışma: Romatoid artrit medial femoral kondiler kıkırdaklarda dejenerasyon ve mobilite kayıbına neden olmaktadır. Bu hastalara erken dönemde eklem koruma tekniklerinin öğretilmesi alt ekstremite dizabilitesini azaltabilecektir.

Anahtar Kelimeler

Diz; Kıkırdak Kalınlığı; Romatoid Artrit; Ultrason

Abstract

Aim: The aim of the present study was to evaluate changes in distal femoral cartilage thickness in patients with rheumatoid arthritis (RA) using ultrasonography. Material and Method: The study enrolled 40 RA patients and 40 age-matched healthy controls. The distal femoral cartilage thickness of the participants was measured by means of ultrasonography. The chair stand test and 10-meter walk test were performed for all participants in order to assess mobility. The Health Assessment Questionnaire was used for evaluation of quality of life and DAS-28 scores for evaluation of the disease activity. Results: Compared to the control group, medial femoral condylar cartilage was thinner bilaterally in patients with rheumatoid arthritis (p<0.05). There was no significant difference between the groups in the cartilage thickness values obtained from the femoral intercondylar area and the lateral femoral condyle. RA patients had a significantly lower performance in the chair stand test and 10-meter walk test versus the control group (p=0.000 and p=0.001, respectively). Physical activity levels were also reduced in RA patients in comparison to the control group (p=0.002). Cartilage thickness measurements did not correlate with any patient characteristics or laboratory parameters. Discussion: Rheumatoid arthritis causes degeneration of medial femoral condylar cartilage and loss of mobility. Providing RA patients with education on joint protection techniques in an early stage would help reduce lower-extremity disability.

Keywords

Cartilage Thickness; Knee; Rheumatoid Arthritis; Ultrasonography

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Introduction

Rheumatoid arthritis (RA) is a progressive rheumatic disease that is characterized by chronic inflammation of synovial tissue in the diarthrodial joints [1]. This condition causes substantial cartilage degradation and joint deformities as a result of the formation of pannus tissue due to synovial inflammation [2]. Patients with rheumatoid arthritis are known to be affected by considerable involvement of the knee joint and resulting severe functional loss [3].

Cartilage loss related to RA is traditionally identified through demonstration of narrowing of the joint space by radiography. However, this method fails to adequately show early changes in the joint and also poses additional risks associated with exposure to radiation [4]. Being an inexpensive, non-invasive, safe, and easy to access method, ultrasound (US) has been increasingly used in recent years [5,6]. Ultrasonography was demonstrated to be a valid modality for evaluation of distal femoral cartilage thickness [4]. Ultrasonographic femoral cartilage examinations are known to have strong correlation with histological grading [7].

Distal femoral cartilage thickness was assessed in various conditions including certain rheumatic diseases: ankylosing spondylitis [8], systemic sclerosis [9], Behçet's disease [10], systemic lupus erythematosus (SLE) [11], and knee osteoarthritis [6].

Our literature search showed that changes in femoral cartilage thickness were not adequately examined in RA patients. There is only one study in the literature that compares femoral cartilage thickness in RA patients versus healthy controls, and no study is available on factors associated with cartilage thickness in these patients [12]. In the current study, we aimed to evaluate changes in distal femoral cartilage thickness by means of ultrasound and to investigate factors associated with cartilage thickness in RA patients.

Material and Method

Forty patients with RA who were being followed and treated at our Physical Therapy and Rehabilitation outpatient clinics were enrolled in the study. RA was diagnosed according to the 2010 ACR/EULAR diagnostic criteria [13]. Patients with previous joint or soft tissue surgery, prior treatment with corticosteroid injections to the knee joint, congenital or traumatic knee problems, or a severe neurological, cardiac, pulmonary, or malignant disease were excluded. Forty healthy subjects matched for age and body mass index (BMI) were enrolled as the control group. Approval for the conduct of the study was obtained from the local ethics committee of our hospital. All patients and control subjects gave informed consent prior to initiation of the study.

Demographic and clinical characteristics including age, height, body weight, disease duration, history of knee pain, and use of medications were recorded for all patients. Range of motion of both knees was measured using a goniometer. Physical examinations were performed to determine the presence of swelling and warmth in the knees. DAS-28 scores were calculated to assess disease activity in the group of RA patients. Serum C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) in 1 hour were obtained for all patients. Quality of life of patients was evaluated using the Health Assessment Questionnaire (HAQ) [14].

The chair stand test (CST) was performed to assess functional mobility in the patient and control groups. For the test, the subject was asked to sit in an upright position at the center of a chair with a seat height of 43 cm with hands placed on the contralateral shoulders. The subject was instructed to sit down on and stand up from the chair for 30 seconds following the "Start" command. The test score was determined based on the number of chair stands during 30 seconds. The ten meter walk test was conducted to evaluate the walking performance of the participants over a short distance. For this purpose, the time required to briskly walk a 10-m distance was recorded. For each subject, the average of three measurements was used in the analysis.

The International Physical Activity Questionnaire-Short Form (IPAQ) was administered to all participants in order to determine their physical activity levels. This questionnaire addresses the time spent in vigorous and moderate activities and walking in the previous 7 days. To obtain activity scores reflected by MET (Metabolic Equivalent of Task), the time (in minutes) spent for a specific activity was multiplied by 8 for vigorous physical activities, by 4 for moderate physical activities, and by 3.3 for walking. Scores for vigorous, moderate, and mild activities were summed to obtain the total physical activity score in METs [15].

Distal femoral cartilage thickness was measured using a Mindray DC-T6 (China) ultrasound device and a 5-10 MHz linear probe. Since femoral cartilage thickness shows a diurnal variation, cartilage thickness measurements were conducted in the morning between 8 and 9 AM for all participants [16]. Measurements were obtained in the supine position with the knee in maximal flexion by placing the probe on the suprapatellar region in the axial position. The thicknesses of the medial femoral condylar (MFC), intercondylar area (ICA), and lateral femoral condylar (LFC) cartilage were measured in both knees (Figure 1). Video images of the cartilage thickness were recorded by

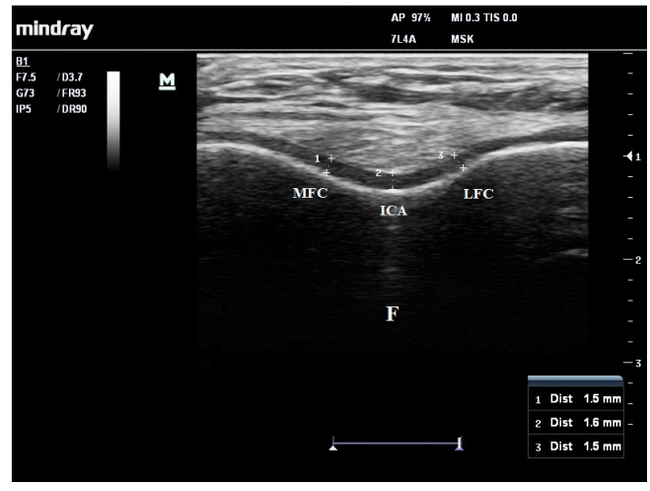

Figure 1. Ultrasonographic image demonstrating the sites of femoral cartilage thickness measurements (F: Femur, ICA: Intercondylar area, LFC: Lateral femoral condyle, MFC: Medial femoral condyle)

the US device. Subsequently, recorded video images of all patients were interpreted by a physiatrist experienced in musculoskeletal ultrasound in order to standardize cartilage thickness measurements; cartilage thickness values were also obtained. Measurements were repeated three times for both knees and

the averaged cartilage thickness values (in millimeters) were used in the analysis.

Statistical analyses

Statistical analyses of the study findings were performed using SPSS (Statistical Package for the Social Sciences) for Windows version 19.0. For analysis of study data, descriptive statistical methods (mean, median, standard deviation, minimum-maximum) were used as well as Student-t test for between-group comparisons of normally distributed quantitative data and Mann-Whitney U test for between-group comparisons of non-normally distributed quantitative data. Results were interpreted at a 95% confidence interval with the significance level set at p<0.05.

Results

Characteristics of both groups are presented in Table 1. Mean age, gender distribution, and mean BMI values were not different between the groups. The disease duration ranged from 1 to 35 years in RA patients. Knee pain was present in 29 RA patients (72.5%). ESR, CRP, HAQ scores, and median DAS-28 values of the RA group are shown in Table 1. Thirty-three patients were receiving Disease-Modifying Anti-Rheumatic Drugs (DMARDs), 4 patients were on anti-tumor necrosis factor (TNF) treatment, and 3 were receiving combination therapy.

The mean chair stand test scores of RA patients were found to be lower than those in the control group, at a highly statistically significant level (p=0.000). The time to complete the 10-meter walk test was significantly longer in RA patients (p=0.001) (Figure 2). The RA group had significantly lower median IPAQ scores with a MET of 99 (min-max: 16.5-495) compared to the control group (median 396, min-max:20-1782) (p=0.002).

Femoral cartilage thickness measurements of a total of 160 knees (both right and left) were analyzed for the two groups. Relative to the control group, the RA group showed thinner MFC cartilage in both right and left knees. However, cartilage thickness measurements of ICA and LFC were not different between groups (Table 2).

Table 1. Characteristics of study groups

	RA (n=40)	Control (n=40)	P value
Age,mean±SD, years	53.9±9.6	51.1±8.8	0.278
Gender (female), n(%)	35 (87.5%)	34 (85%)	0,745
BMI, mean±SD, kg/m2	29.0±5.3	27.5±4.4	0.307
Disease duration, years	6 (1-35)[a]		
Knee pain, n(%)	29 (72.5%)		
ESR, mm/h	29.5 (5-59)[a]		
CRP, mg/L	0.35 (0.1-4.1)[a]		
DAS-28	2.92 (1.2-4.8)[a]		
HAQ	0.6 (0.1-1.75)[a]		
Treatment, n(%)			
DMARD	33 (82.5%)		
Anti-TNF	4 (10%)		
DMARD+Anti-TNF	3 (7.5%)		

[a] Median (minimum-maximum), BMI: body mass ındex, CRP: c-reactive protein, DAS-28: disease activity score-28, DMARD: disease-modifying anti-rheumatic drug, ESR: eritrosit sedimentation rate, HAQ: health assessment questionnaire, SD: standard deviation, TNF: tumor necrosis factor

Femoral cartilage thickness was not correlated with age, BMI, duration of disease, disease activity, HAQ scores, or laboratory tests among RA patients (p > 0.05).

Table 2. Comparisons of femoral cartilage thickness between study groups

	RA (n=40)	Control (n=40)	P value
MFCR, mm	1.7±0.25	1.9±0.24	0.015 *
ICAR, mm	1.9±0.29	2.0±0.20	0.518
LFCR, mm	1.9±0.24	2.0±0.19	0.416
MFCL, mm	1.7±0.24	1.9±0.19	0.015 *
ICAL, mm	1.9±0.28	2.0±0.17	0.426
LFCL, mm	1.9±0.25	2.0±0.18	0.415

p<0.05 * ,ICA: intercondylar area, L: left, LFC: lateral femoral condyle, MFC: medial femoral condyle, mm: millimeter, RA: rheumatoid arthritis, R: right

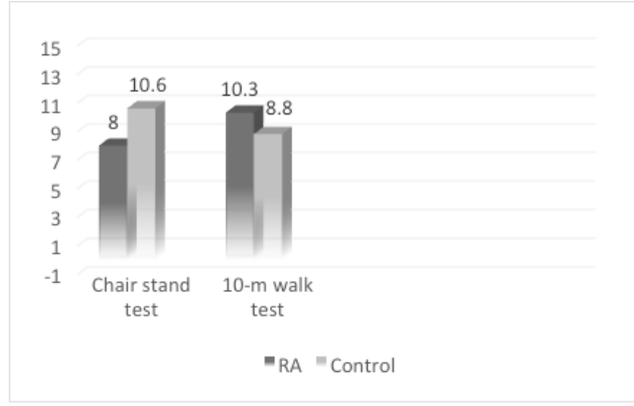

Figure 2. Comparisons of chair stand and 10-meter walk test scores between study groups

Discussion

Our present study showed a reduction in the medial femoral cartilage thickness in RA patients. Compared to healthy individuals, distal femoral cartilage thickness was shown to be reduced in patients with Behçet's disease, which causes arthritis of the knee and wrist [10]. In that study, thinning of LFC and ICA was demonstrated only in the left knee but, similar to our study findings, MFC thickness was reduced in both knees. The thinning of cartilage among patients with Behçet's disease, particularly in the medial femoral cartilage, was considered to be associated with early degeneration of the knee joints and eventually with osteoarthritis [10].

Reduction of femoral cartilage thickness was also demonstrated in systemic sclerosis, another autoimmune inflammatory disease [9]. In that study, while bilateral ICA cartilage thickness measurements were similar to those of control subjects, thinning of the LFC cartilage was observed only in the left knee and thickness of the MFC cartilage was reduced in both knees; these results are consistent with our findings [9]. It is known that during mechanical loading, the load is transferred particularly through the medial femorotibial compartment at the knee joint because of the knee abduction moment [16]. Specifically, medial joint spaces are affected in patients with knee osteoarthritis. The reductions in MFC cartilage thickness observed in our RA patients seem to be associated with development of secondary osteoarthritis in these patients.

Kaya et al. [11] found that the femoral cartilage thickness was comparable between patients with SLE and healthy subjects.

However, they reported that cartilage thickness was increased in the SLE group when only the patients receiving corticosteroids were taken into account. The authors concluded that this might be attributed to an increase in chondrogenesis induced by steroid use. Among patients with ankylosing spondylitis, femoral cartilage was shown to be protected in those patients receiving anti-TNF therapy due to suppression of inflammation; these patients had thicker femoral condylar cartilage in comparison to patients not using anti-TNF agents [8].

Our study is the first to report the association of femoral cartilage thickness with clinical and laboratory parameters in RA patients. Batmaz et al. [8] did not find any correlations between clinical and laboratory parameters and femoral cartilage thickness in AS patients. In a separate study, similar findings were reported for patients with Behçet's disease [10]. Our findings from RA patients also showed the absence of correlations between femoral cartilage thickness and age, disease duration, DAS-28, HAQ scores, ESR, and CRP levels. According to Malas et al. [18], among patients with knee osteoarthritis, those with severe clinical manifestations were not different from those with a mild clinical course with respect to the cartilage thickness. On the other hand, femoral cartilage thickness was shown to be negatively correlated with age in healthy individuals [17].

The synovium is one of the major target sites of inflammation in RA and similar rheumatic disorders. Cytokines such as interluekin-1 (IL-1) and TNF-α which are increased in the serum and synovial fluid in the course of RA have also been reported to induce the catabolism of chondrocytes in patients with osteoarthritis [19]. Marked increases in the molecules implicated in structural cartilage damage, such as matrix metalloproteinases, are known to be increased in RA patients [20]. Infiltration of inflammatory cells, primarily cytokines, into the synovial tissue and release of lytic enzymes into the environment through the actions of inflammatory mediators result in progressive cartilage destruction [1]. There is evidence that TNF-α and IL-1 are also involved in the pathogenesis of osteoarthritis as a result of similar actions [21]. Severe knee joint degenerations and increased prevalence of total knee arthroplasty have been shown in RA patients, especially in the presence of greater disease activity. Patients on long-term treatment with steroids alone without concomitant methotrexate were reported to have a higher risk for total knee arthroplasty [3]. It was reported that involvement of a large joint and particularly the knee joint could be the initial predictor of a severe disease course associated with subsequent significant destruction in smaller joints in RA patients [22].

Limitations of our study include the cross-sectional design and small sample size. Further studies are needed to evaluate the impact of different therapies on femoral cartilage thickness in larger patient groups with RA.

Based on reductions in the distal femoral cartilage thickness observed in patients with rheumatoid arthritis and on literature data on other inflammatory rheumatic diseases, it seems that early cartilage degeneration occurs in the course of these diseases, mainly affecting the medial joint cartilage. Inclusion of joint protection techniques including weight control and management of the activities of daily living as part of the treatment regimen would help decrease lower-extremity disability in these patients who experience significant functional loss due to joint deformities.

Competing interests

The authors declare that they have no competing interests.

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