Ultrasonographic Evaluation of Femoral Cartilage Thickness in Patients with Ankylosing Spondylitis

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ABSTRACT

Objective: *To evaluate femoral cartilage thickness in patients with ankylosing spondylitis (AS) by using ultrasonography.*

Methods: *Eighty-four patients (55 M, 29 F) with a diagnosis of AS and 84 age-, gender- and body mass index-matched healthy subjects were enrolled. Demographic and clinical characteristics of the patients including disease duration, morning stiffness and medications were recorded. The femoral cartilage thicknesses of both knees were measured with a 7–12 MHz linear probe while subjects' knees were held in maximum flexion. Three mid-point measurements were taken from both knees (lateral femoral condyle (LFC), intercondylar area (ICA) and medial femoral condyle (MFC)).*

Results: *Concerning both ICA (*$p < 0.001$*) and left MFC (*$p = 0.013$*), cartilage measurements were significantly thicker in AS patients than control subjects. In a subgroup analysis (anti-tumour necrosis factor (TNF) users vs anti-TNF naive) cartilage thickness measurements – bilateral ICA (*$p = 0.000$*) and left MFC (*$p = 0.017$*) – were found to be greater in AS patients under anti-TNF treatment (*$n = 65$*) when compared with those of healthy controls.*

Conclusion: *We imply that AS patients seem to have thicker femoral cartilage, which could be related to anti-TNF treatment.*

Keywords: Ankylosing spondylitis, femoral cartilage, thickness, ultrasound

Evaluación Ultrasonográfica del Espesor del Cartílago Femoral en Pacientes con Espondilitis Anquilosante

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RESUMEN

Objetivo: *Evaluar el grosor del cartílago femoral en pacientes con espondilitis anquilosante (EA) mediante el uso de la ultrasonografía.*

Métodos: *Se reclutaron ochenta y cuatro pacientes (55 M, 29 F) con un diagnóstico de EA y 84 sujetos saludables apareados por edad, género e índice de masa corporal. Se registraron las características demográficas y clínicas de los pacientes, incluyendo medicamentos, rigidez matutina, y duración de la enfermedad. Los espesores del cartílago femoral de ambas rodillas se midieron con una sonda lineal de 7–12 MHz mientras que los sujetos sostenían sus rodillas en máxima flexión máxima. Se llevaron a cabo tres mediciones de punto medio desde ambas rodillas: cóndilo femoral lateral (CFL), área intercondílea (AIC), y cóndilo femoral medial (CFM).*

Resultados: *En relación tanto en AIC (*$p < 0.001$*) como en CFM izquierdo (*$p = 0.013$*), las mediciones del cartílago fueron significativamente de mayor grosor en los pacientes con EA que en los sujetos del control. En un análisis de los subgrupos (usuarios de anti-TNF frente a pacientes anti-TNF-ingenuos), se halló que las mediciones del espesor del cartílago – AIC bilateral (*$p = 0.000$*) y CFM izquierdo (*$p = 0.017$*) – fueron mayores en pacientes bajo tratamiento anti-TNF (*$n = 65$*) en comparación con aquellas de los controles sanos.*

Conclusión: *Eso implica que los pacientes con EA tienen al parecer un cartílago femoral más grueso, lo cual podría estar relacionado con el tratamiento anti-TNF.*

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Palabras claves: Espondilitis anquilosante, cartílago femoral, grosor, ultrasonido

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INTRODUCTION

Ankylosing spondylitis (AS) is a chronic, progressive, inflammatory disease of the axial skeleton, large peripheral joints and entheses (1). Fibrosis and secondary ossification can result in complete ankylosis of the involved joints, leading to severe disability (2).

Recently, it has been reported that cartilage may be the primary target of the immune response in spondyloarthropathy. Furthermore, cartilage directed cellular autoimmunity might play an important role in joint-specific tissue damage in patients with AS (3). However, to the best knowledge of the authors, femoral cartilage (an important component of the weight bearing mechanism of a disabled) has not been studied in existing literature.

As such, the purpose of this study was two-fold – to find out whether femoral cartilage thicknesses of AS patients were any different from those of healthy controls and explore whether those measurements were associated with disease characteristics of the subjects or with their radiological damage scores. In this regard, we used musculoskeletal ultrasound which has been previously shown to be a valid and reliable method for evaluating femoral cartilage (4–8).

SUBJECTS AND METHODS

Eighty-four patients (55 M, 29 F) with a diagnosis of AS were enrolled in the study. The diagnosis of AS was based on the modified 1984 New York criteria (9). Patients were recruited from Physical and Rehabilitation Medicine departments of three centres between January and March 2013. Cartilage measurements pertaining to the age, gender and body mass index (BMI) matched 84 healthy subjects were acquired from the authors' previously recorded pool of data. The study procedure was explained to each and every patient and they gave written consent to participate. The protocol was approved by one of the attending centres' local ethics committee.

Patients with any of the following were excluded: collagen tissue disorders or other inflammatory articular diseases, previous knee surgery, malignancy, chronic kidney, liver or thyroid disease and pregnancy.

Demographic and clinical characteristics of the patients including disease duration (defined as the duration since the onset of the first symptoms of AS), morning stiffness and medications were recorded. Pain was evaluated by a 10 cm visual analogue scale (VAS). Laboratory testing comprised complete blood count, liver/renal function tests, erythrocyte sedimentation rate (ESR) and serum C-reactive protein (CRP).

Ultrasound measurements were performed bilaterally with a linear probe (7–12 MHz Logiq P5, GE Medical Systems, USA). While subjects comfortably sat on the examination table with their knees in maximum flexion, the probe was placed in an axial position on the suprapatellar area; the distal femoral cartilage was visualized as a strongly anechoic structure between the sharp bony (femur) cortex and the suprapatellar fat (Figure). Three mid-point measurements – lateral femoral condyle (LFC), intercondylar area (ICA) and medial femoral condyle (MFC) – were taken from each knee.

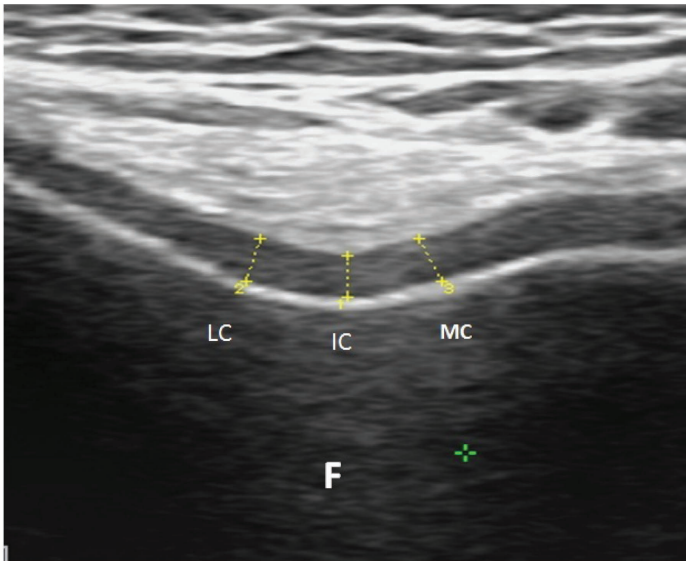

Figure: Ultrasonographic image (suprapatellar axial view) demonstrating the femoral cartilage measurements (LC: lateral condyle, IC: intercondylar area, MC: medial condyle, F: femur).

Disease activity and functional status were evaluated by the Turkish versions of the Bath AS Disease Activity Index [BASDAI] (10) and the Bath AS Functional Index [BASFI] (11), respectively. The Bath AS Metrology Index [BASMI] (12) was used for spinal and hip assessment. Radiological damage was scored from the anteroposterior pelvis and lateral cervical/lumbar radiographies using the Bath AS Radiology Index [BASRI] (13).

SPSS version 15.0 was used for statistical analyses. Data were expressed as mean ± standard deviation. Paired samples *t*-test was used to compare the mean knee cartilage thickness values between the groups. Chi-squared test was used for frequencies of smoking status. Correlations between patients' characteristics and femoral cartilage thickness measurements were analysed using Pearson's correlation coefficients. Statistical significance was set at $p < 0.05$.

RESULTS

Measurements regarding 168 knees of 84 AS patients (55 M, 29 F) and 168 knees of 84 age, gender and BMI matched healthy subjects were taken into analysis. The demographic and clinical characteristics of the patients are shown in Table 1. Mean age of the patients and controls were 34.5 ± 7.9

Table 1: Clinical characteristics of the patients (n = 84)

Characteristics	Mean ± SD
Age (years)	34.5 ± 7.9
BMI (kg/m^2)	25.3 ± 4.4
Disease duration (month)	36.5 ± 47.6
Duration of symptom onset (month)	58.2 ± 61.4
BASDAI	3.2 ± 1.9
BASFI	4.5 ± 1.9
BASMI	3.2 ± 2.7
BASRI	5.5 ± 2.6

BMI: body mass index, BASDAI: Bath Ankylosing Spondylitis Disease Activity Index, BASFI: Bath Ankylosing Spondylitis Functional Index, BASMI: Bath Ankylosing Spondylitis Metrology Index, BASRI: Bath Ankylosing Spondylitis Radiology Index

years. Body mass index values of the patients and controls were 25.3 ± 4.4 kg/m^2 and 25.0 ± 3.3 kg/m^2, respectively ($p > 0.05$).

Mean femoral cartilage thickness values of the patients and controls are shown in Table 2. Compared with those of the controls, cartilage measurements were significantly thicker at both ICA ($p < 0.001$) and left MFC ($p = 0.013$) in patients with AS. There was no correlations between cartilage thickness measurements and patients' characteristics (age, history of smoking, duration of disease, BMI, BASMI, BASDAI, BASRI, BASFI) or laboratory tests ($p > 0.05$).

Table 2: Comparison of femoral cartilage thickness measurements (cm)

	Patients (n = 84)	**Controls** (n = 84)	***p***
Right LFC	0.22 ± 0.4	0.21 ± 0.4	0.787
ICA	0.25 ± 0.6	0.21 ± 0.5	**0.000**
MFC	0.22 ± 0.4	0.21 ± 0.4	0.072
Left LFC	0.21 ± 0.4	0.21 ± 0.4	0.112
ICA	0.24 ± 0.7	0.21 ± 0.4	**0.000**
MFC	0.23 ± 0.5	0.21 ± 0.4	**0.013**

LFC: lateral femoral condyle, ICA: intercondylar area, MFC: medial femoral condyle

In a subgroup analysis (anti-tumour necrosis factor (TNF) users and anti-TNF naive), cartilage thickness measurements – bilateral ICA ($p = 0.000$) and left MFC ($p = 0.017$) – were found to be higher in AS patients under anti-TNF treatment (n = 65) when compared with those of healthy controls.

DISCUSSION

The results of this study showed that femoral cartilage seems to be thicker in patients with AS than healthy controls. Further, AS patients who were under anti-TNF treatment had thicker femoral cartilage thickness values than those without anti-TNF treatment.

Several biomarkers of articular cartilage have been shown to predict structural damage. They include matrix metalloproteinases (MMPs), especially MMP-1 and MMP-3 in rheumatoid arthritis (RA) and osteoarthritis (14, 15). Moreover, one report has described elevated levels of MMP-3 in AS patients with concomitant peripheral joint synovitis (16). Matrix metalloproteinase-1 can degrade type II collagen in articular cartilage and MMP-3 can activate pro-MMP-1 (17). It has also been shown that these markers decrease following treatment with anti-TNF-α therapies in patients with RA (17, 18). Despite the involvement of cartilage structures in AS, the number of the studies focussing on the relationship between anti-TNF-α treatments with cartilage structure is even less (16). Further, it has been known for a long time that TNF-α increases the breakdown of the extracellular matrix of articular cartilage, while inhibiting its synthesis (19, 20). Likewise, anti-TNF-α agents may influence cartilage metabolism in way decreasing type II collagen degradation and increasing aggrecan turn-over in AS patients as well (21, 22). In this sense, we reasoned that the knee joint cartilage might have somewhat been protected by anti-TNF in our patients. On the other hand, we could not find any correlation between cartilage thickness values and patient characteristics, and we believe that this might be attributed to the small sample size. Another limitation of this study would be its cross-sectional design. Nonetheless, our findings seem to be noteworthy. Yet, apart from a wide range of studies on ultrasound imaging of AS patients, we believe that there are no data regarding their femoral cartilage and that our preliminary findings would shed light on future investigations.

CONCLUSIONS

Overall, the findings of this study imply that AS patients seem to have thicker femoral cartilage, which could be related to anti-TNF treatment. In addition to previous reports that mentioned the favourable effects of anti-TNF-α on chondrogenesis, we suggest that further studies encompassing larger samples and with longer disease duration are needed to clarify the scenario in AS.

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