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ORIGINAL ARTICLE – OPEN ACCESS

Evaluation of Metacarpophalangeal Joint Cartilage Thickness in Patients with Rheumatoid Arthritis: A Clinical and Ultrasonographic Study

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ABSTRACT

Objective: This study aims to evaluate the relationship of ultrasonographic cartilage thickness with clinical and functional parameters in patients with rheumatoid arthritis (RA).

Materials and Methods: The study included 50 patients with RA and 20 patients with osteoarthritis (OA), together with 20 healthy subjects. Demographic and clinical characteristics of the patients and the healthy controls were recorded. The second and third metacarpophalangeal (MCP) articular cartilage surfaces were examined in both hands of RA patients. Cartilage qualities were also measured using the semiquantitative scoring system for the quality of MCP joint cartilage. Duruöz Hand Index (DHI) was used to assess the hand functions.

Results: The second and third MCP cartilage thicknesses were found to be less in RA patients than in healthy controls and controls with OA ($p<0.05$). No statistically significant relationship was found between continuous glucocorticoid use and MCP cartilage thickness or semiquantitative scoring ($r=0.125$, $p=0.154$; $r=0.172$, $p=0.103$; respectively). There was a statistically significant correlation between disease duration, delay time in diagnosis, DHI scores, and the second MCP and third MCP cartilage thicknesses, as well as between the second MCP and third MCP semiquantitative scores ($p<0.05$).

Conclusion: Thickness of the MCP joint cartilage is significantly lower in patients with RA who experienced a prolonged delay in diagnosis than that in RA patients who adhere to the management and in RA patients.

Keywords: Cartilage, hand strength, metacarpophalangeal joint, rheumatoid arthritis, ultrasonography

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INTRODUCTION

Rheumatoid arthritis (RA) is an autoimmune inflammatory disease in which cartilage, ligament, and tendons are infiltrated by inflammatory cells and pannus tissue. This alteration leads to the disability of the joints as a result of cartilage and bone erosion, ligament degradation, and tendon ruptures (1). Impaired articular mobility develops as a result of hand deformity in RA patients who are not diagnosed and treated in the early period. The most commonly affected joints are the small joints in the hands and the feet (2). Hand and wrist involvement that may occur in the early and late periods leads to limitations in hand movements and disrupts the daily life activities of the patients (3).

Musculoskeletal ultrasonography (US) is a reliable and valid method in the assessment of the small joints of the hand. US produces comparable results to magnetic resonance imaging (MRI) in the measurement of small hand joint cartilage thickness (4). It has been demonstrated that the cartilage thicknesses measured via US in the metacarpophalangeal (MCP) and proximal interphalangeal (PIP) joints correlate with the joint spacing measured by conventional radiography (5). Reduction in hand functions, reduction of grip strength, and disability in RA patients have been studied extensively (6–8). However, there is quite a few research regarding hand functions in association with the deterioration of cartilage structure.

In our study, we aimed to evaluate the relationship of ultrasonographic MCP cartilage thickness with clinical and functional parameters in patients with RA.

MATERIALS and METHODS

The study was planned to be prospective and cross-sectional. The control and patient groups were matched based on age and gender. Patients were recruited from outpatient rheumatology clinics. Patients with cancer, those who were pregnant or in the recent postpartum period (6 months), those who were undergoing hand surgery, and those who were taking a local steroid injection in the MCP were excluded. A total of 20 healthy participants who met the exclusion criteria, including relatives of healthcare professionals working in our hospital, included in the current study.

Ethics committee approval for our study and informed consent from all participants was obtained from the local ethics committee of the Faculty of Medicine, Sakarya University, with an approval date of June 05, 2014, and an issue number of 71522473/050.01.04/49.

Fifty RA patients in remission according to the Disease Activity Score 28 (DAS 28) were included in this study (9). The disease activity of the patients was evaluated using the DAS28 measure, in which 28 joints are evaluated. These criteria include C-reactive protein (CRP), number of swollen joints, number of tender joints, and patient global health score. Fifty patients, who were fulfilled with RA according to the RA ACR-EULAR 2010 criteria (10) not later than 1 year before, were included in our study. Twenty patients, who were diagnosed with hand osteoarthritis (OA) according to ACR 1990 criteria (11) and 20 healthy individuals, who did not have an inflammatory rheumatic disease affecting the cartilage metabolism, were included in our study as the control group.

Patients were allowed to use biological or synthetic disease-modifying antirheumatic drugs (DMARDs) or low-dose glucocorticoids. The patients were reviewed in terms of whether they use glucocorticoids continuously or from time to time. Patients in clinical remission for at least 6 months were included in the study. Regular treatment was defined as patients who regularly visited doctors at least every 3 months. Those who missed a doctor's visit for more than 6 months were considered to have received irregular treatment.

Demographic and clinical characteristics of the patients and the healthy controls, such as age, gender, body mass index (BMI) (kg/m^2), diagnosis date, date of onset of the first symptom, and the time elapsed from the onset of the first symptom until the diagnosis, were recorded. The delay time in diagnosis was defined as the time elapsed from the onset of the first symptom until the diagnosis. Duruöz Hand Index (DHI), which is based on patient reporting, was used to assess hand functions (12). DHI consists of 18 questions that are scored between 0 and 90 points assessing the daily life, coordination, and upper extremity functions. Health assessment questionnaire (HAQ) disability index (13), which consists of 20 questions, was used for the quality of life assessment. Laboratory assessments included complete blood count, erythrocyte sedimentation rate (ESR), CRP, rheumatoid factor (RF), and anticyclic citrullinated peptide (anti-CCP) antibody.

Patients, who cannot flex their fingers at an angle of 90°, who cannot move their MCP joints to a neutral position, and who have swollen MCP joints and fixed deformity were not included in our study.

US Scanning

A US machine (Venue 40; GE Healthcare, Germany) with a multifrequency linear array probe (7–15 MHz) was used. US was performed by two ultrasonographers, one of whom had 10 years of musculoskeletal system US experience and the other had 5 years of experience. The second and third MCP articular cartilage surfaces were examined in both hands of the patients. The distance between the subchondral bone surface, which gives a sharp reflection, and the cartilage surface, which gives less reflection, was measured in the measurement of the cartilage thickness. The thickest distance along the cartilage surface was considered in the measurement of the distance. Measurements were made in two ways: from the dorsal side, while the MCP joints were flexed at 90°, and from the volar side, while the MCP joints were in the neutral position with a longitudinal view (Fig. 1). Cartilage thicknesses were calculated based on the mean values of dorsal and volar measurements. Patients with synovial effusion or synovial proliferation that prevented cartilage thickness measurement were excluded from the study (Fig. 2).

In our study, using the semiquantitative scoring system defined by Mandl et al. (14) for the quality of MCP joint cartilage, cartilage qualities were also measured. Based on this scoring system, regular cartilages were classified as grade 0 cartilages, those with focal thinning or focal loss were classified as grade 1 cartilages, and those with diffuse thinning or diffuse loss were classified as grade 2 cartilages.

Statistical Analysis

SPSS statistical software (IBM SPSS statistic version 20.0) was used for all statistical analyses. Quantitative variables (clinical, laboratory, and US results) were presented using mean, standard deviation (SD), median values, and ranges. To determine the number of samples to be included in this study, a power analysis was performed; α=0.05 and 1 – β=0.80 yielded a sample size of 40. The statistical power was 0.80. The normality of the distribution of the data in the groups was confirmed using the Kolmogorov–Smirnov test. Relationships between categorical values were analyzed using a one-way analysis of variance (ANOVA) and Pearson correlation test. The Kruskal–Wallis test and Mann–Whitney U test were performed to compare continuous variables, and the chi-squared test was performed to compare categorical variables. A multiple linear regression analysis was used to calculate the occurrence of second and third MCP cartilage thicknesses for factors with a significance level of $p<0.1$ in univariate analysis. P values of <0.05 were accepted to indicate statistical significance. Unweighted kappa statistics were used to calculate interobserver agreement in the assessment of MCP joint cartilage thickness and semiquantitative scoring.

RESULTS

Demographic and Clinical Characteristics of Patients and The Healthy Controls

There was no statistically significant difference between the group of RA patients and the control group of OA patients and healthy subjects in terms of age, gender, and BMI values (p=0.184, p=0.561, and p=0.582, respectively). Table 1 summarizes the main demographic and clinical characteristics and laboratory results of the patient group consisting of 50 RA patients and the control group consisting of 20 OA patients and 20 healthy controls.

Of the RA patients, 82% (n=41) were determined to have made regular hospital visits after being diagnosed with RA; 66% (n=33) were determined to have been using conventional synthetic DMARDs; 16% (n=8) were determined to have been using biological DMARDs; 8% (n=4) were determined to have been using both conventional synthetic and biological DMARDs; and 62% (n=31) were determined to have been using glucocorticoids; and 50% (n=25) were determined to have been using glucocorticoids continuously.

Relationship between US Findings and Clinical Status

No statistically significant relationship was found between continuous glucocorticoid use and MCP cartilage thickness or semiquan-

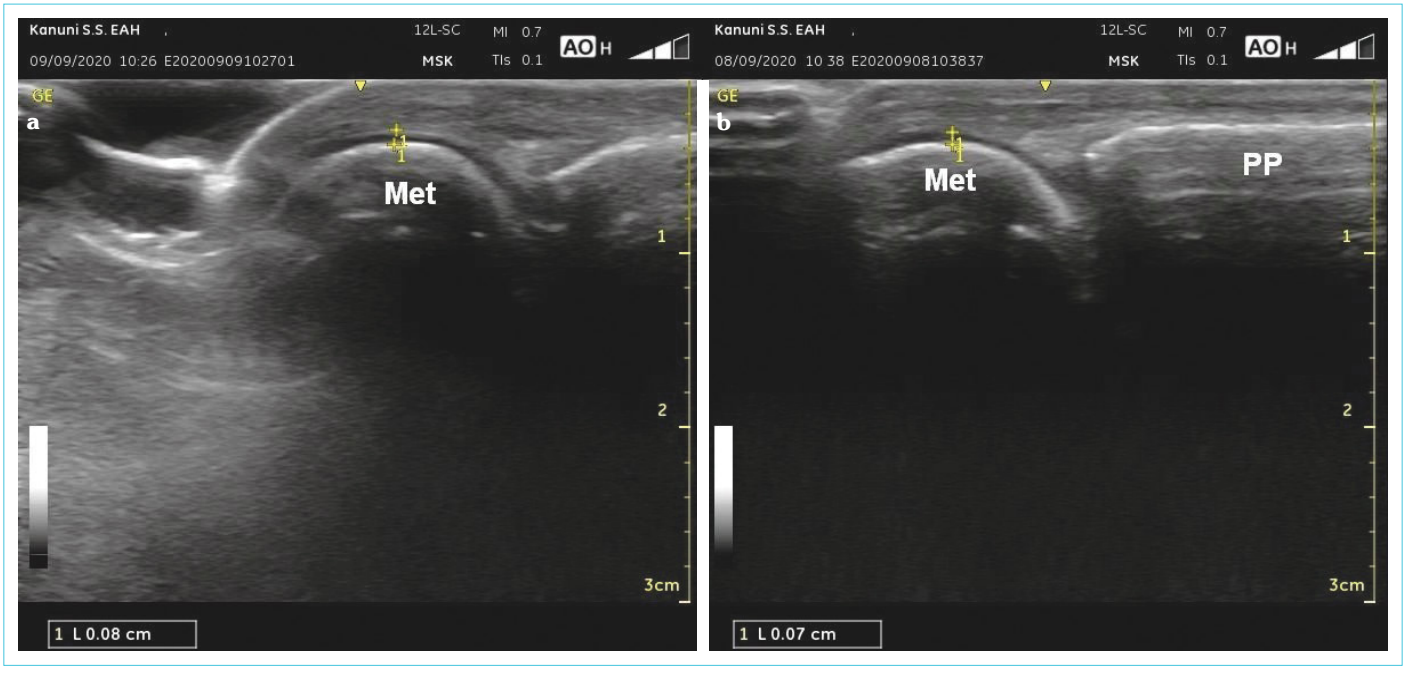

Figure 1. MCP cartilage thicknesses from the dorsal side with a transverse view (a) and volar side with a longitudinal view (b)
MCP: Metacarpophalangeal, PP: Proximal interphalangeal

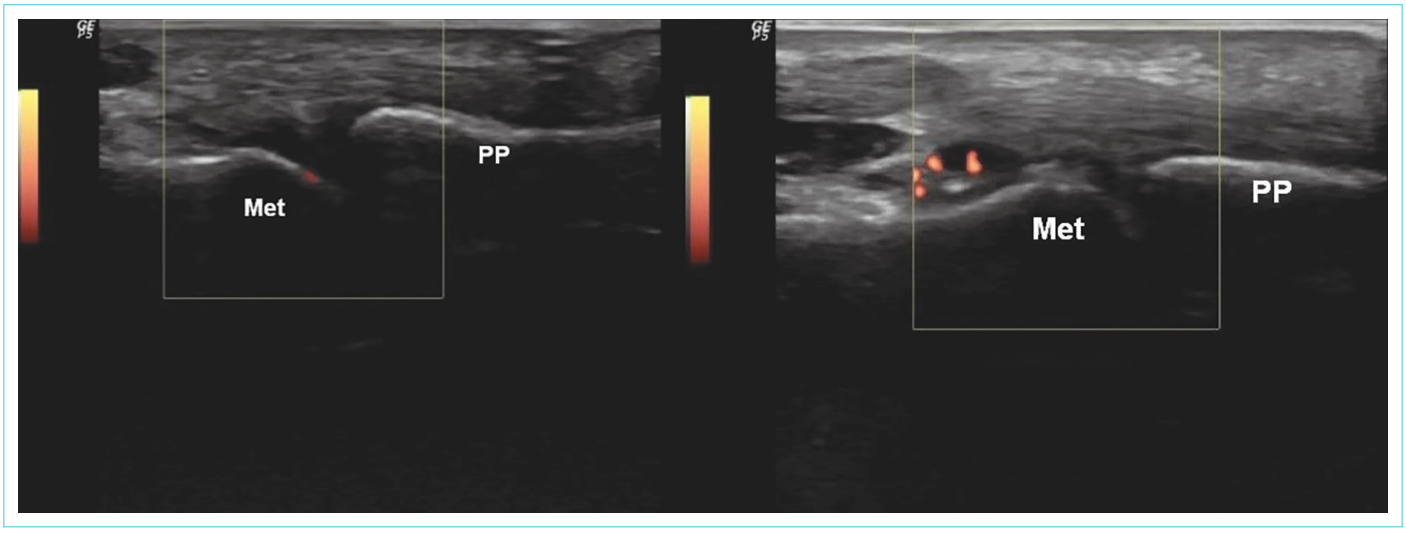

Figure 2. Patients excluded from the study due to synovial effusion or synovial proliferation that prevented cartilage thickness measurement
Met: Metacarpophalangeal, PP: Proximal interphalangeal

titative scoring (r=0.125, p=0.154; r=0.172, p=0.103; respectively). The second and third MCP cartilage thicknesses were found to be higher in patients who receive regular treatment (r=0.367, p=0.009; r=0.326, p=0.021; respectively). There was a statistically significant correlation between disease duration, delay time in diagnosis, DHI scores, and the second MCP and third MCP cartilage thicknesses, as well as between the second MCP and third MCP semiquantitative scores (Table 2).

Multiple regression analysis of the relationship between the second MCP cartilage thickness and clinical parameters revealed a significant correlation between the second MCP cartilage thickness and delay time in diagnosis and DHI (p=0.012, p=0.027; respectively), whereas multiple regression analysis of the relationship between the third MCP cartilage thickness and clinical parameters revealed a significant correlation between the third MCP cartilage thickness and DHI only (p=0.008) (Table 3).

Interobserver Reliability

K-values were (respectively) 0.94 and 0.95 for the MCP joint cartilage thickness and semiquantitative scoring.

DISCUSSION

US is a noninvasive and inexpensive diagnostic method that provides information to the clinician in the early period in terms of

Table 1. Clinical, laboratory, and ultrasonographic characteristics of study patients

	RA patients (n=50)	OA patients (n=20)	Healthy subjects (n=20)	p1	p2	p3	p across categories
Age (years), mean±SD	51.32±10.30	53.71±2.71	49.80±9.33	0.121	0.254	0.241	0.087
Sex							
Male	86	90	90	0.152	0.125	0.378	0.652
Female	14	10	10				
BMI (kg/m^2)	28.36±4.09	27.24±3.45	28.08±2.98	0.547	0.541	0.345	0.541
Time elapsed from first clinical symptoms, mean±SD months	7.19±6.69	NA	NA				
Time elapsed after diagnosis, mean±SD months	6.59±6.41	NA	NA				
Delay in diagnosis, mean±SD, years	0.60±0.83	NA	NA				
Duration of clinical remission, mean±SD years	1.13±0.76	NA	NA				
DAS 28 scores, mean±SD	2.17±0.25	NA	NA				
HAQ total scores, mean±SD	5.26±4.25	NA	NA				
Duruöz Hand index, mean±SD	9.13±8.59	NA	NA				
RF positivity, % patients	82/18	NA	NA				
Anti-CCP positivity, % patients	82/18	NA	NA				
ESR, mean±SDmm/h	12.15±10.43	NA	NA				
CRP, mean±SD mg/dl	6.66±9.56	NA	NA				
25-OH Dvit, mean±SD	19.15±12.57	NA	NA				
Cartilage thickness (mm) (median, min-max)							
2. MCP	0.5 (0–1.1)	0.7 (0.5–0.8)	0.7 (0.5–1)	0.006	0.001	0.726	0.001
3. MCP	0.6 (0–1)	0.7 (0.4–0.9)	0.7 (0.5–1)	0.008	0.001	0.359	0.001
2. MCP semiquantitative score							
grade 0	16	55	95				
grade 1	60	45	5	0.007	0.001	0.003	0.001
grade 2	24	0	0				
3. MCP semiquantitative score							
grade 0	24	55	85				
grade 1	62	45	15	0.001	0.001	0.031	0.001
grade 2	14	0	0				

P represents the significance of the three group comparisons. Post hoc group comparisons were defined as follows: p1: RA patients vs. healthy subjects, p2: RA patients vs. OA patients, and p3: OA patients vs. healthy subjects. The Kruskal–Wallis test and Mann–Whitney U test were performed to compare continuous variables, and the chi-squared test was performed to compare categorical variables. RA: Rheumatoid arthritis; OA: Osteoarthritis; SD: Standard deviation; BMI: Body mass index; DAS 28: Disease Activity Score 28; HAQ: Health Assessment Questionnaire; RF: Rheumatoid factor; Anti-CCP: Anticyclic citrullinated peptides; ESR: Erythrocyte sedimentation rate; CRP: C-reactive protein; MCP: Metacarpophalangeal; NA: Not available

early diagnosis, treatment follow-up, and damage imaging in RA. In our study, we aimed to find the factors that may be associated with ultrasonographic cartilage damage in RA patients. The results of our study revealed that the time of diagnosis and the delay time in diagnosis are the most important factors that affect the MCP cartilage thicknesses measured by US. MCP cartilage thickness was found to be less in RA patients than in healthy controls and controls with OA. Our study is the only study that investigates the relationship between MCP cartilage thicknesses and hand functions in RA patients. Another important result of our study is that the semiquantitative scoring system was found to yield comparable results with those of the quantitative measurement in terms of MCP cartilage thickness measurement.

RA is an inflammatory arthropathy that can involve multiple joints in the body; however, most characteristically it involves small joints such as MCP, PIP, and wrist. MCP joint involvement has a negative effect on hand functions in particular. In our study, MCP cartilage thickness was found to be less in RA patients than in control groups of healthy subjects and OA patients. The median value of cartilage thickness in RA patients was found to be 0.5 and 0.6 mm. In comparison, Ogura et al. found the median value of MCP cartilage thickness as 0.5 mm, Möller et al. found the MCP cartilage thicknesses within the range of 0.0 and 0.7 mm, and Mandl et al. found the mean cartilage thickness as 0.69 mm (5–16). Our results are consistent with the existing literature, and we calculated the cartilage thickness based on both

Table 2. Correlation of ultrasonographic measurements with clinical parameters

	Cartilage thickness		Semiquantitative score	
	2. MCP	**3. MCP**	**2. MCP**	**3. MCP**
Age	–0.155	–0.319*	–0.244	–0.296
Height	0.137	0.223	–0.057	–0.208
Weight	0.166	0.023	–0.068	–0.112
BMI	0.122	–0.024	–0.053	–0.025
Disease duration	–0.460**	–0.517**	0.271*	0.416**
Delay in diagnosis	–0.413**	–0.309*	0.290*	0.318*
DAS 28-CRP	0.109	–0.105	0.210	–0.105
HAQ	0.053	0.152	–0.072	0.115
Duruöz Hand Index	–0.445**	0.537**	0.295*	0.386*

Values are shown as correlation coefficients (r); bold values indicate statistically significant values; Relationships between categorical values were analyzed using one-way analysis of variance (ANOVA) and Pearson correlation test. *: Correlation is significant at the 0.05 level (two-tailed); **: Correlation is significant at the 0.01 level (two-tailed). MCP: Metacarpophalangeal; BMI: Body mass index; DAS 28: Disease activity score 28; CRP: C-reactive protein; HAQ: Health assessment questionnaire

volar and dorsal measurements for a more accurate result. Our results indicate that the use of only dorsal measurement would have been sufficient in the calculation of cartilage thickness. Cartilage thickness measurement in clinical practice emerges as a time-consuming and laborious method. Assessment of the cartilage semiquantitatively has been reported to be less time-consuming and to have yielded similar results with the measurement of cartilage thickness (16). Findings of Ogura et al. have also been confirmed by our results. Saltzherr et al. suggested a result of their MRI-based study that OA may lead to cartilage erosion in the MCP joint (16, 17). In our study, we have not found any difference between the cartilage thicknesses of OA patients and of the healthy subjects; however, we have found based on semiquantitative scoring that the OA patients have thinner cartilage tissue compared to the healthy subjects. Consequently, ultrasonographic measurement of cartilage thickness in the second and less frequently third MCP joints from the dorsal and volar sides of these fingers, besides improving the delay in diagnosis in patients with suspected RA, can guide early treatment of RA, stop the progression of structural changes, and help patients to preserve their hand functions accordingly.

In the literature, studies that investigate MCP joint cartilage thicknesses in RA patients are few, and studies that examine the relationship between clinical findings and cartilage thickness are even fewer. Mitra et al., in their study involving Juvenile Idiopathic Arthritis patients, found that wrist cartilage thickness was not affected by the duration of the disease. It has been reported in similar studies that there has been more thinning in patients with systemic and polyarticular forms in knee joint cartilage thickness than in oligoarticular patients (18, 19).

Multiple regression analyses of our results suggest that it is the delay time in diagnosis, not the diagnosis date, that increases the erosion of the MCP articular cartilage. To our best knowledge, this is a new finding. As the duration of the disease increases, due to the nature of the disease, cytokine release is increased and synovial proliferation is formed, which leads to a destructive effect on cartilage and results in a reduction in the cartilage thickness. Not only an increase in the duration of the disease but also an increase in the time elapsed without any treatment leads to more cartilage loss in the first years of the disease.

The effect of long-term use of low-dose glucocorticoids on disease activity has been discussed, especially in recent years (20). In our study, we also found that the cartilage thickness of patients who regularly use glucocorticoids is higher. This may actually seem surprising, given the negative effects of glucocorticoid treatment on cartilage metabolism. However, we believe that the result we obtained indirectly shows the positive effects of glucocorticoid and regular DMARD treatment on disease activity.

It has been previously demonstrated in many studies that hand functions are more impaired in patients with RA than in the healthy population (21, 22). A decrease in hand grip strength is one of the important parameters that objectively indicate hand disability (23). Conditions such as different muscle groups in the upper extremity, limitations in joint mobility, deformities, and joint pain are some of the factors that are known to affect hand functions. The method

Table 3. Multivariate analysis of the factors associated with second and third MCP cartilage thicknesses in patients with rheumatoid arthritis

Dependent variable	**R^2 (adjusted)**	**Independent variables**	**B**	**ß**	**p**
2. MCP cartilage thickness	0.345	Constant	0.072		0.000
		Disease duration	–0.001	–0.209	0.171
		Delay in diagnosis	–0.010	–0.340	0.012
		Duruöz Hand Index	–0.001	–0.325	0.027
3. MCP cartilage thickness	0,379	Constant	0		
		Disease duration	–0.001	–0.279	0.063
		Delay in diagnosis	–0.050	–0.201	0.117
		Duruöz Hand Index	–0.001	–0.387	0.008

To determine the independent predictors of the second and third MCP cartilage thicknesses, the independence of variables was determined by entering any significant variables from the univariate analysis into multiple linear regression analysis. MCP: Metacarpophalangeal

that best reflects hand functions is the hand grip strength. Hand grip occurs mainly in two forms, namely, pinching and power grips. The second and third fingers have an important place in both pinching and power grips. DHI assessment includes daily life activities related to both pinching and power grips. Rydholm et al. (22) found that patients with MCP synovitis had less hand grip strength than patients with synovitis in the wrist and elbow. The decrease we have observed in our study in the thickness of the MCP cartilage is an indirect effect of intensely experiencing MCP synovitis. One of the striking results of our study is that patients with reduced cartilage thickness were found to have poor hand functions as measured using DHI.

Our study had some limitations. These limitations are that the number of patients included in our study was relatively low and that our ultrasonographic assessment was limited to the second and third MCP joints. The fact that our study has not been tested in terms of intraobserver agreement, although it has yielded good results when tested in terms of the interobserver agreement, can be considered to be another limitation.

CONCLUSION

The thickness of the MCP joint cartilage is significantly lower in patients with RA who experienced a prolonged delay in diagnosis than in patients with RA who adhere to the management. Our study suggests that reduction in MCP joint cartilage thickness is an important factor in hand disability. Our study will shed light on studies that are to be conducted in a similar design with larger-scale ultrasonographic assessments.

Ethics Committee Approval: The Sakarya University Faculty of Medicine Ethics Committee granted approval for this study (date: 05.06.2014, number: 71522473/050.01.04/49).

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

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – NK, HH; Design – HH; Materials – NK, HH; Data Collection and/or Processing – NK; Analysis and/or Interpretation – HH; Literature Search – NK; Writing – NK, HH.

Conflict of Interest: The authors have no conflict of interest to declare.

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