

## Relationship between shoulder ultrasound findings and disease activity in patients with rheumatoid arthritis: A pilot study

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### ABSTRACT

**Objectives:** The aim of this study was to investigate whether shoulder ultrasound (US) findings were associated with disease activity and pain level in rheumatoid arthritis (RA) patients.

**Patients and methods:** Between April 2019 and November 2019, a total of 60 shoulders of 30 female patients with RA (mean age: 53.8±12.0 years; range, 30 to 65 years) were included. The patients were questioned about shoulder pain and their Disease Activity Score-28 (DAS28) was estimated. After clinical examination with shoulder impingement tests, both shoulders were evaluated by US.

**Results:** Of 60 shoulders examined by shoulder US, the most common shoulder pathology was supraspinatus tendinopathy (n=33, 55%). The prevalence of subdeltoid bursitis on US was significantly higher in the group with moderate disease activity, compared to the group with low disease activity (p<0.05). There were no significant differences in the physical examination findings of patients with low and moderate disease activity. In terms of US findings, subscapularis tendinopathy, glenohumeral joint and acromioclavicular joint degeneration, and subacromial bursitis were more common in shoulders with a history of pain, compared to non-painful shoulders.

**Conclusion:** Shoulder US may be useful for demonstrating shoulder involvement in patients with RA, independent of the presence of shoulder pain.

**Keywords:** Disease activity score, rheumatoid arthritis, shoulder joint, ultrasound.

Rheumatoid arthritis (RA) is a chronic, progressive autoimmune disease influenced by both genetic and environmental factors and characterized by inflammation of the synovial joints and tendon sheaths.<sup>1</sup>

Synovitis leads to progressive damage to cartilage, bones, and joints. This damage results in severe functional limitations and impaired quality of life. Although synovial tissues are the main site of involvement, extraarticular systemic

involvement can also occur. The prevalence of RA in the adult population varies between 0.5 and 0.8%, the average female-to-male ratio is 3:1, and 80% of patients are between the ages of 35 and 50 years.<sup>2</sup> It is important to quickly obtain a diagnosis to initiate management as early as possible.<sup>3</sup>

Shoulder pain is one of the most common musculoskeletal problems in RA patients within two years of diagnosis. Shoulder tenderness and

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swelling are seen rarely in early stage of RA; however, erosive damage at the shoulder develop in majority of patients with RA over the years.<sup>4</sup>

Pain in the shoulder may be caused by various intra- and extraarticular pathological mechanisms in RA patients.<sup>5</sup> Determining the exact source of the pathology is more difficult in RA patients due to the presence of other concomitant musculoskeletal diseases.<sup>6</sup>

In the diagnosis and follow-up of RA, direct radiography plays an important role in detecting joint involvement. However, direct radiography alone is not sufficient to detect shoulder involvement. Ultrasound (US) evaluation of the musculoskeletal system enables the exact source of pain to be identified.<sup>7</sup> Studies have shown that US is superior to direct radiography in detecting joint erosions. Ultrasound can be used to evaluate synovitis, tenosynovitis, and bursitis.<sup>8,9</sup> In addition, it is a non-invasive, non-irradiating, rapid, low-cost technique that allows comparative examination in the same session, it is one of the first imaging methods that should be applied in patients presenting with shoulder pain and shoulder joint limitation, after history-taking, physical examination, and direct radiography.<sup>10</sup>

Although shoulder pain and shoulder US evaluations in RA patients have been performed in previous studies, to the best of our knowledge, there is no study in the literature showing an association between disease activity score and shoulder involvement. In the present study, we aimed to determine the relationship between shoulder US findings and disease activity in RA patients with and without shoulder pain.

## PATIENTS AND METHODS

This prospective study was conducted at Kütahya Health Sciences University, Department of Physical Medicine and Rehabilitation between April 2019 and November 2019. A total of 60 shoulders of 30 female patients (mean age:  $53.8 \pm 12.0$  years; range, 30 to 65 years) diagnosed with RA were included in the study. The patients met the 2010 American College of Rheumatology (ACR) criteria<sup>11</sup> and were under follow-up for RA for at least one year.

A written informed consent was obtained from each patient. The study protocol was approved by the Kütahya Health Sciences University Interventional Ethics Committee (date-no: February 06, 2019-2019/02-1). The study was conducted in accordance with the principles of the Declaration of Helsinki.

### Patients

Female patients who were 30 to 65 years of age, were followed for RA for the last year, and had no shoulder movement limitation were included in the study. Exclusion criteria were history of shoulder injections or surgery, presence of systemic comorbidity such as chronic renal failure or malignancy, history of disease that may affect the central nervous system and functional performance, poor cooperation, and presence of systemic comorbidity that may cause shoulder involvement (e.g., diabetes mellitus).

The patients first underwent clinical evaluation of upper extremity muscle strength, shoulder joint range of motion, shoulder-specific tests (Hawkins, Yergason, Neer, Jobe, Patte, Gerber Lift Off), Disease Activity Score-28 (DAS28), the Arm Shoulder Hand Problems Questionnaire (DASH), and the Health Assessment Questionnaire (HAQ). After clinical evaluation, US examination was performed by a different researcher who was blinded to the patients' clinical findings.

### Procedures

Collection of demographic data and the physical examination were performed by the same clinician. The patients' age, sex, height, weight, disease duration, medications used, and number of affected joints were questioned, body mass index was calculated, and the DAS28 was applied. Neurological examination was performed, including upper extremity muscle strength, sensory examination, and deep tendon reflex evaluation. Both shoulders were evaluated using the Hawkins, Yergason, Neer, Jobe, Gerber Lift Off and Patte tests.

In the Hawkins test, the patient's arm was forcibly rotated inward, while the shoulder and elbow were in 90° flexion. In the Neer test, the patient's scapula was stabilized with one hand and the arm was forced into passive forward flexion with the other hand. In the Yergason test, with the patient's elbow at 90° flexion, the bicipital

groove of the shoulder was palpated with one hand, while the forearm was grasped with the other hand. The patient was asked to supinate her forearm against the resistance applied. In the Jobe test, the patient was asked to resist downward resistance applied, while the arm was at 90° abduction and 30° adduction with internal rotation. In the Patte test, the patient was asked to perform external rotation against resistance, while the arm was at 90° abduction and elbow at 90° flexion. In the Gerber Lift Off test, the patient's arm was positioned in extension and internal rotation with the back of the hand on the hip. The patient pushed her hand horizontally, while resistance was applied from the opposite direction.<sup>12</sup> The sensitivity of these impingement tests reportedly ranges from 63 to 97% and specificity for these tests ranges from 24 to 96%. The sensitivity of the tension-based provocative test reportedly ranges from 50 to 76% with a specificity range of 87 to 96%.<sup>13</sup> Disease activity was evaluated using the DAS28. The DAS28 is calculated based on the number of tender and swollen joints, the patient's global self-assessment (on a 0-100 mm Visual Analog Scale [VAS]), and acute phase reactant levels. The DAS28 <2.6 was classified as remission, 2.6-3.2 as low disease activity, 3.3-5.1 as moderate disease activity, and >5.1 as high disease activity.<sup>14,15</sup>

The patients' general health status was evaluated using the HAQ. This instrument examines activities of daily living in eight areas (dressing and personal care, arising, eating, walking, hygiene, reach, grip, and common activities), each scored between 0 (cannot do at all) and 3 points (can do easily). All scores are summed and divided by 8.<sup>16</sup> The Turkish validity and reliability study of the HAQ was conducted by Küçükdeveci et al.<sup>17</sup> The Disabilities of the Arm, Shoulder, and Hand (DASH) questionnaire consists of a total of 30 questions in three sections. Twenty-one questions evaluate the patient's difficulty in activities of daily living, five questions evaluate presence and type of pain, and the remaining four questions evaluate social function, sleep, work, and the patient's self-confidence. Each question is scored between 1 and 5, where 1 indicates the absence of that problem/symptom and 5 indicates the

highest level of that problem/symptom. The Turkish validity and reliability of the DASH were conducted by Düger et al.<sup>18</sup>

Bilateral shoulder US examination using a 6 to 18 Mhz linear probe (Mindray-UMT 200, United States) was performed by another clinician who was experienced in musculoskeletal ultrasonography and blinded to the patients' clinical evaluation findings. The patients were seated on a stool during the examination, while the examiner stood or sat on higher stool. The shoulder US examination consisted of evaluation of the biceps tendon, subscapularis tendon, supraspinatus and infraspinatus muscles, rotator cuff, glenohumeral (GH) joint, acromioclavicular (AC) joint, and subacromial and subdeltoid bursa according to a standard protocol.<sup>19</sup> The biceps tendon was examined with the arm in adduction, forearm resting on the thigh and palm supinated. After checking whether the tendon was in the bicipital groove in the transverse plane, the tendon was visualized along the longitudinal axis and followed to examine for abnormalities. The patient's shoulder was brought to 90° external rotation with elbow at 90° flexion and the probe was slid medially along the humerus to examine the insertion of the subscapularis tendon on the lesser tuberosity. The supraspinatus tendon was examined after bringing the arm into adduction with hyperextension and internal rotation (hand on back pocket position). This position was maintained while examining the subacromial and subdeltoid bursa. The infraspinatus tendon was visualized by moving the probe posteriorly with the arm in neutral position. Internal and external rotation of the shoulder facilitated infraspinatus examination. The GH joint was also visualized in this way. The AC joint was imaged in the coronal plane with the arm in neutral position.

In biceps tendonitis, a hypoechoic area more than 2 mm in thickness was observed surrounding the biceps tendon. The absence or discontinuity of the supraspinatus, infraspinatus, or subscapularis tendons was evaluated as full-thickness tear; reduced tendon homogeneity or limited focal defects on the articular or bursa surface of the tendon as partial tear; and diffuse thickening of the tendon as tendinosis. Fluid accumulation causing more than 2 mm widening of the subacromial-subdeltoid bursa

**Table 1.** Demographic and clinical data of patients (n=30)

	n	%	Mean±SD
Age (year)			53.8±12.0
Weight (kg)			76.9±14.5
Height (cm)			160.3±6.3
Body mass index (kg/m <sup>2</sup> )			30.0±5.9
Disease duration (year)			11.9±11.7
Erythrocyte sedimentation rate (mm/h)			21.7±14.2
C-reactive protein (mg/dL)			7.6±6.6
RF-positive	14	46.7	
DMARD use	26	87	
Steroid use	15	50.0	
Biologic agent use	5	16.7	
DAS28			3.4±1.0
HAQ			1.2±0.5
DASH			43.0±21.4
≥1 shoulder pathology on US (%)	28	93.3	

SD: Standard deviation; RF: Rheumatoid factor; DMARD: Disease-modifying anti rheumatic drug; DAS28: Disease Activity Score 28; HAQ: Health Assessment Questionnaire; DASH: Disabilities of the Arm, Shoulder, and Hand; US: Ultrasound.

was considered consistent with bursitis. Rotator cuff tear was diagnosed in the presence of non-homogeneous echogenicity, discontinuity, and disrupted rotator cuff contour. Bone erosion, fluid, and hypertrophic changes were considered signs of AC joint and GH joint involvement.

### Statistical analysis

Statistical analysis was performed using the IBM SPSS for Windows version 22.0 software (IBM, Corp., Armonk, NY, USA). Continuous variables were expressed in mean ± standard

deviation (SD), while categorical variables were expressed in number and frequency. Categorical variables were analyzed using the chi-square test. A *p* value of <0.05 was considered statistically significant.

## RESULTS

The mean erythrocyte sedimentation rate was 21.7±14.2 mm/h, mean C-reactive protein value was 7.6±6.6 mg/dL, and 46.7% of the patients were rheumatoid factor (RF)-positive. Twenty-six (87%) patients were under treatment with a disease-modifying anti-rheumatic drug (DMARD), 15 (50%) patients with steroid, and five (16.7%) patients with a biological agent. Twenty (66.7%) patients had involvement of ≥3 peripheral joints. Based on the US evaluation, 28 (93.3%) patients had pathological findings in at least one shoulder, while 16 (53.3%) patients had bilateral findings. In the 60 shoulders examined by US, the most common shoulder pathology was supraspinatus tendinopathy (33 shoulders, 55%). Baseline demographic and clinical data of the patients are shown in Table 1.

The patients reported a history of shoulder pain in 24 shoulders (painful group) and no history of shoulder pain in 36 shoulders (non-painful group). When these two groups were compared based on physical examination findings, painful shoulders had significantly higher rates of Neer, Hawkins, Jobe, Gerber, and Patte test positivity compared to the non-painful shoulders (Table 2). Based on the US findings, subscapularis tendinopathy,

**Table 2.** Comparison of clinical test results according to pain history

Clinical tests	Painful (n=24)		Non-painful (n=36)		<i>p</i>
	n	%	n	%	
Positive Neer's sign	15	62.5	11	30.5	0.014*
Positive Hawkins' sign	16	66.6	10	27.7	0.003*
Positive Jobe's sign	11	45.8	7	19.4	0.029*
Positive Gerber's sign	8	33.3	2	5.5	0.025*
Positive Patte's sign	8	33.3	2	5.5	0.007*
Positive Yergason's sign	4	16.6	1	2.7	0.078

\* *p*>0.05.

**Table 3.** Comparison of ultrasound findings according to pain history

Pathology	Painful (n=24)		Non-painful (n=36)		p
	n	%	n	%	
Biceps brachii tendinopathy	6	25.4	7	19.4	0.420
Subscapularis tendinopathy	11	45.8	5	13.9	0.007*
Supraspinatus tendinopathy	16	66.7	17	47.2	0.111
Infraspinatus tendinopathy	6	25.0	6	16.7	0.319
GH joint degeneration	15	62.5	9	25.0	0.004*
AC joint degeneration	16	66.7	14	38.9	0.032*
Subacromial bursitis	12	50.0	9	25.0	0.044*
Subdeltoid bursitis	5	20.8	5	13.9	0.357

GH: Glenohumeral; AC: Acromioclavicular; \* p>0.05.

**Table 4.** Comparison of clinical test results by disease activity level

Clinical tests	Moderate disease activity (n=34)		Low disease activity (n=26)		p
	n	%	n	%	
Positive Neer's sign	16	47.1	10	38.5	0.344
Positive Hawkins' sign	18	52.9	8	30.8	0.072
Positive Jobe's sign	12	35.3	6	23.1	0.231
Positive Gerber's sign	5	14.7	2	7.7	0.339
Positive Patte's sign	8	23.5	2	7.7	0.098
Positive Yergason's sign	3	8.8	2	7.7	0.628

**Table 5.** Comparison of shoulder ultrasound findings according to disease activity level

Pathology	Moderate disease activity (n=34)		Low disease activity (n=26)		p
	n	%	n	%	
Biceps brachii tendinopathy	9	26.5	4	15.4	0.239
Subscapularis tendinopathy	11	32.4	5	19.2	0.276
Supraspinatus tendinopathy	17	50.0	16	61.5	0.438
Infraspinatus tendinopathy	5	14.7	7	26.9	0.332
GH joint degeneration	11	32.4	13	50.0	0.132
AC joint degeneration	18	52.9	12	46.2	0.578
Subacromial bursitis	14	44.1	6	23.1	0.115
Subdeltoid bursitis	9	26.5	1	3.8	0.020*

GH: Glenohumeral; AC: Acromioclavicular; \* p>0.05.

GH joint and AC joint degeneration, and subacromial bursitis were more common in painful shoulders compared to non-painful shoulders (Table 3).

As there were no patients with remission or high disease activity scores, there were two groups regarding disease activity scores as moderate disease activity group (n=34) and low

disease activity group (n=26). Comparison of shoulder physical examination findings between these two groups showed no significant differences (Table 4). Based on the US findings, the prevalence of subdeltoid bursitis was significantly higher in the moderate disease activity group. No significant differences were detected in other pathology findings (Table 5).

## DISCUSSION

This study evaluated 60 shoulders of 30 women with RA. Based on the US examination, 28 (93.3%) patients had findings of at least one shoulder pathology. Shoulder pain is one of the most common complaints encountered in RA patients.<sup>9</sup> Nearly half of RA patients have tenderness in their shoulder joints and 30% of them have decreased shoulder function one year following RA onset.<sup>20</sup> In a study of 37 RA patients with a mean disease duration of 7.5 years, this rate was reported to be 83.8%.<sup>4</sup> At the end of 12 years, 96% of the patients were diagnosed with erosive damage at the shoulder.

Our patients showed a higher prevalence of shoulder joint involvement due to their mean disease duration of 11.9 years. Ultrasound findings seen in RA may differ according to the patient group and disease duration. Of note, RA affects the large joints more than the peripheral joints in the later stages of the disease.<sup>20</sup> In a study evaluating 44 hospitalized RA patients with a mean disease duration of 12 years, subacromial bursitis was the most frequent finding, followed by GH joint synovitis.<sup>21</sup> In another US study evaluating 100 patients with RA with a mean disease duration of 4.5 years, 14 patients presented with involvement of the GH joint and 22 with inflammatory abnormalities of the subacromial bursa.<sup>22</sup>

Different results were obtained in the studies examining the prevalence of shoulder pathology in patients with RA. In a study examining 90 shoulders of RA patients, involvement of the long head of the biceps tendon was reported in 32.2% and subacromial bursitis in 17.7%.<sup>6</sup> Another study reported the supraspinatus tendon as the most frequent site of rupture in RA patients.<sup>23</sup> Besides, the most common findings

were supraspinatus tendinopathy, humeral erosions, and biceps tenosynovitis in a recent study.<sup>24</sup> We also observed the highest rate of pathology in the supraspinatus tendon (55%) in our study. Similarly, the most affected tendon was the supraspinatus in the Guillen-Astete et al.'s study.<sup>25</sup> However, in another study by Kim et al.,<sup>9</sup> the subscapularis tendon showed the highest rate of pathology. This discrepancy in our results may be due to the inclusion of patients with a longer disease duration, mild and moderate disease activity according to DAS28, and the smaller number of patients in our series.

The patients in this study were divided into two groups, those with low and moderate disease activity based on their DAS28 values. Pathological findings were more common in patients with moderate DAS28 scores; however, only the difference in subdeltoid bursitis was statistically significant. Although higher disease activity was associated with RA involvement of all joints, the significant difference in subdeltoid bursitis only was attributed to most patients having shoulder involvement, regardless of disease activity.

As most RA patients have periarticular lesions affecting the subacromial-subdeltoid bursa and GH joint,<sup>26</sup> physical examination may have lower sensitivity and specificity. In addition, shoulder involvement in RA patients may be accompanied by elbow and wrist joint involvement, making it difficult for the patient to describe the location of pain. In the present study, there was no significant relationship between the patients' DAS28 values and their shoulder test results. However, painful shoulders had significantly higher positivity rates in all tests, except for Yergason, demonstrating a correlation between shoulder pain and positive clinical test results. Since the clinical tests used in this study were pain provoking tests, it was a reasonable result. Besides, US findings supported these findings by indicating more involvement in patients with shoulder pain.

Subacromial tendinopathy, GH joint and AC joint degeneration, and subacromial bursitis were more common in painful shoulders. The shoulder was the painful area in this study. Since pain is one of the most common symptoms of degenerative shoulder diseases, it was more commonly observed in the painful group. Also, a

long-standing inflammatory process in the course of the RA can cause degenerative changes.

Although shoulder US examination is not routine in RA patients, US is frequently performed to demonstrate the presence of synovitis in hand joints.<sup>8,9</sup> In a comparative study of radiography, US, and magnetic resonance imaging (MRI) examinations in RA patients, US could detect more bone erosions than conventional radiography. However, MRI was significantly more sensitive than US in detecting synovitis, tenosynovitis, and bursitis as well as bone erosions.<sup>8</sup> In the present study, MRI was not routinely performed, but patients who had severe shoulder pathology and required a detailed examination were referred for MRI.

In the current study, our findings indicate that shoulder joint involvement may be also common in patients without pain, and RA patients should be questioned about shoulder joint pain. The lack of a healthy control group is one of major limitation of current study. The small patient number, long disease duration, and the use of only US instead of routine MRI for diagnosis are the other limitations of this study.

In conclusion, shoulder joint involvement is a common finding in patients with RA. Shoulder joint destruction in RA patients gradually occurs, resulting in decreased function. To avoid the joint destruction, early detection of inflammation in the shoulder joints is necessary. Based on our study findings, there is no relationship between the level of disease activity level (low or moderate) and shoulder pathology involvement. Besides, US examination reveals pathological findings in RA patients with no shoulder pain. This suggests that musculoskeletal US examination is valuable in the diagnosis and follow-up of RA patients. However, further large-scale, well-designed studies are needed to confirm these findings.

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