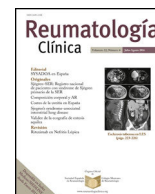




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Original article

Rotator cuff tendinopathy is associated with increased activity score in rheumatoid arthritis



Jorge Medina-Castillo^a, Rodrigo J. Castillo-de la Garza^a, David Vega-Morales^{b,*},
Jorge A. Esquivel-Valerio^a, Axel A. De León-Pérez^a, Lorenia De La Cruz-Becerra^a,
Alondra Elizabeth Montoya-Montes^b, Lourdes Gil-Flores^b, Dionicio Ángel Galarza-Delgado^a

^a Hospital Universitario "Dr. Jose Eleuterio Gonzalez", Universidad Autonoma de Nuevo Leon (Rheumatology Service), Monterrey (Nuevo Leon), Mexico

^b IMSS Hospital General de Zona No. 17 (Rheumatology and Infusion Center), Monterrey (Nuevo Leon), Mexico

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ABSTRACT

Introduction and objective: Rheumatoid arthritis (RA) is often accompanied by musculoskeletal (MS) symptoms, which can hinder the diagnosis of concurrent conditions like rotator cuff tendinopathy (RCT), the most common cause of shoulder pain. Undiagnosed RCT in patients with RA may be associated with higher disease activity scores. This study aimed to assess the difference in these scores between RA patients with and without RCT, considering ultrasound pathological findings.

Methods: We conducted a cross-sectional, observational, comparative study in patients with shoulder pain who met the 2010 ACR-EULAR classification criteria for RA between January 2022 and January 2023. The measurements of Disease Activity Score based on 28 joints using C-Reactive Protein (DAS28-CRP), Erythrocyte Sedimentation Rate (DAS28-ESR), and the Clinical Disease Activity Index (CDAI) were used to evaluate RA activity, while functional capacity was assessed using the Health Assessment Questionnaire Disability Index (HAQ-DI). The Disabilities of the Arm, Shoulder, and Hand questionnaire (DASH) and shoulder ultrasound examination was performed to detect the presence or absence of RCT.

Results: Patients with RCT had greater mean scores on DAS28-CRP (5.23, 1.28 vs. 3.08, $p < 0.001$), and DAS 28-ESR (5.43, SD = 1.28 vs. 3.66, $p < 0.001$). VAS median scores were higher in the RCT group (70.00 vs. 2.00, $p < 0.001$). By ultrasound 12 patients (21%) had acromioclavicular synovitis. Glenohumeral and acromioclavicular arthrosis was found in both groups. No patients had arthritis in the glenohumeral joint.

Conclusion: RA patients with RCT have higher composite index and disease activity scores than those without RCT. An intentional RCT screening should be recommended for those with shoulder pain and elevated disease activity.

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La tendinopatía del manguito rotador se asocia con aumento de la puntuación de la actividad en artritis reumatoide

RESUMEN

Introducción y objetivo: La artritis reumatoide (AR) puede acompañarse de síntomas musculoesqueléticos, lo que enmascara el diagnóstico de condiciones concurrentes como la tendinopatía del manguito rotador (TMR). La TMR en pacientes con AR puede asociarse con puntajes más altos de actividad de la enfermedad. El objetivo es evaluar la diferencia de estas puntuaciones en pacientes con AR con y sin TMR.

Metodología: Se realizó un estudio observacional, transversal y comparativo en pacientes con dolor de hombro que cumplían los criterios de clasificación ACR-EULAR 2010 para AR entre enero de 2022 y enero de 2023. Se utilizaron el Índice de Actividad de Enfermedad basado en 28 articulaciones usando la proteína C reactiva (DAS28-PCR), la velocidad de sedimentación globular (DAS28-VSG) y el Índice de

Palabras clave:

Artritis reumatoide
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* Corresponding author.

E-mail address: drdavidvega@yahoo.com.mx (D. Vega-Morales).

Actividad de la Enfermedad Clínica (CDAI) para evaluar la actividad de la AR. La capacidad funcional se evaluó utilizando el Índice de Discapacidad del Cuestionario de Evaluación de la Salud (HAQ-DI). Se aplicó el cuestionario de Discapacidades de Brazo, Hombro y Mano (DASHe) y se realizó un ultrasonido del hombro para detectar TMR.

Resultados: Los pacientes con TMR tuvieron promedios mayores en DAS-PCR (5,23, 1,28 vs. 3,08, $p < 0,001$) y DAS28- VSG (5,43, DE = 1,28 vs. 3,66, $p < 0,001$). Las medianas de la escala visual análoga fueron mayores en TMR (70,00 vs. 2,00, $p < 0,001$). Por ultrasonido, 12 pacientes (21%) tenían sinovitis acromioclavicular. En ambos grupos se encontró artrosis glenohumeral y acromioclavicular. Ningún paciente tenía artritis en la articulación glenohumeral.

Conclusión: Los pacientes con AR y TMR presentan puntajes de actividad más altos que aquellos sin TMR. Se recomienda un cribado en pacientes con dolor de hombro y alta actividad de enfermedad.

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Introduction

Rheumatoid arthritis (RA) is a chronic disease characterized by synovial membrane inflammation with a symmetric polyarticular pattern, resulting in swelling, pain, stiffness, and damage that lead to deformities and functional impairment.¹

Given the heterogeneous nature of RA, disease status assessment is important for achieving optimal outcomes. To evaluate disease activity, tools like Disease Activity Score based on 28 joints (DAS28) and the Clinical Disease Activity Index (CDAI) were developed and are currently used as part of the approach in patients with RA.^{2,3} The DAS28 generates a score based on tender and swollen joints, erythrocyte sedimentation rate (ESR) or C-reactive protein (CRP), and the Visual Analog Scale (VAS) for pain.³ This score can be calculated using either CRP (DAS28-CRP) or ESR (DAS28-ESR). CRP, however, is a more direct marker of inflammation and is more sensitive to short-term changes. Both measurements have a linear relationship, but they are not interchangeable within individuals.⁴

Rheumatic regional pain syndromes (RRPS) are clinical disorders characterized by pain and functional impairment of tendons, ligaments, bursa, or fascia in the appendicular MS system.⁵ Rotator cuff tendinopathy (RCT) represents the most common cause of RRPS,⁶ compromising the stabilization of the glenohumeral joint and impairing shoulder movement.

RCT presents with pain and weakness due to anatomical or functional impairment. It encompasses a variety of shoulder conditions such as tendinitis, tendinosis, subacromial bursitis and shoulder impingement.^{7,8}

Patients with RA have about 50% higher risk of developing rotator cuff disease,⁹ this may be attributed to the chronic inflammation characteristic of the disease, which affects the glenohumeral joint surface.¹⁰ However, it is important to consider that shoulder pain in these patients is not necessarily attributable to RA alone.

Undiagnosed tendinopathy of the shoulder in patients with RA may be associated with poorer outcomes. Therefore, we aimed to assess the difference in disease activity scores between RA patients with RCT and those without it, considering ultrasound pathological findings.

Methods

We conducted an observational, cross-sectional, comparative study from January 2022 to January 2023 in a rheumatology outpatient clinic in a referral hospital. This study was approved by the IRB with the registration number: RE22-00001.

Patients

Patients (age ≥ 18 years) with shoulder pain who met the 2010 ACR/EULAR classification criteria for rheumatoid arthritis¹¹ during the study period were eligible. Exclusion criteria included a prior diagnosis of RCT by clinical examination and a history of adhesive capsulitis/frozen shoulder or peripheral nerve injury associated with shoulder trauma. Patients underwent clinical examination to determine the presence of RCT and were assigned to the RA + RCT group. They were then referred for ultrasound examination. These patients were included consecutively until the target sample size was reached. Subsequently, RA patients without clinical signs of RCT were selected through consecutive convenience sampling and matched by sex and age, forming the RA without RCT group. The matched patients were recruited within the same week as their corresponding counterparts underwent ultrasound. The patient flow is illustrated in Fig. 1. All patients gave consent prior to inclusion in this study.

Rheumatoid arthritis activity, functional assessment and shoulder assessment scores

DAS28-CRP, DAS28-ESR,^{4,12} and CDAI,¹³ were used to evaluate disease activity. RA activity was classified based on DAS28 scores with <2.6 labeled as remission, 2.6 to <3.2 as mild activity, >3.2 to <5.1 as moderate activity, and >5.1 as high activity. The severity of RA was determined by CDAI considering ≤ 2.8 as remission, ≥ 2.8 to 10 as low activity, >10 to ≤ 22 as moderate activity, and >22 as high activity. Functional capacity was assessed by the Spanish version of the Health Assessment Questionnaire Disability Index (HAQ-DI).¹⁴ The Disabilities of the Arm, Shoulder, and Hand questionnaire validated in Spanish tool (DASHe) was applied for shoulder assessment.¹⁵

Shoulder clinical examination

Clinical assessment and clinical test examination were performed to detect the presence or absence of RCT. Clinical tests for RCT included pain provocation tests, strength tests, and composite tests for pain or weakness. A subacromial or rotator cuff disorder was considered positive if shoulder pain was elicited between 60° and 120° degrees while performing a painful arc test. Rotator cuff muscle strength was evaluated by the "Drop arm test" for the supraspinatus, the internal rotation lag test for the subscapularis, the external rotation lag test for the supraspinatus and infraspinatus, and the external rotation resistance test for the infraspinatus muscles.

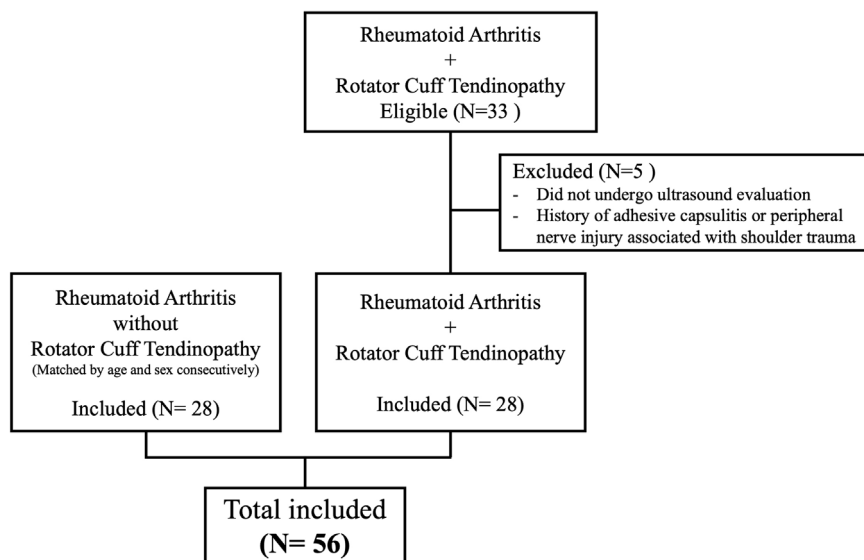


Fig. 1. Patient flow diagram.

Ultrasound

A musculoskeletal ultrasound (MSUS) examination of both shoulders was performed using the scanning technique proposed by the 2017 EULAR standardized procedures for ultrasound imaging in rheumatology.¹⁶ MSUS was performed with MyLab50[®] Xvision equipped with a 5/7.5/10 MHz Mindray 7L4a linear probe, guided by an MSUS expert who was blinded to patients' clinical and laboratory data at the time of the examination. Imaging was required to differentiate and verify RCT from disease activity. The anterior, lateral, and posterior aspects of the joint were scanned. Synovitis was defined according to the published definitions of Outcome Measures in Rheumatology (OMERACT).¹⁷ Cases of joint effusion, acromioclavicular synovitis, or glenohumeral synovitis were attributed to RA activity. Representative ultrasound images are shown in Figs. 2 and 3 illustrating findings in a patient with RA without RCT and another with RA + RCT, respectively

Sample size calculation

We conducted a two-sample mean test with an alpha level of 0.05 and a power of 0.80. Based on the DAS28 score as the variable, the minimum detectable difference between the means was set at -1.2, with a mean of 4.2 for group 1 (patients with RA and shoulder tendinopathy) and 3.0 for group 2 (patients with RA without shoulder tendinopathy).¹⁸ Based on these parameters, the required sample size per group was 26.

Statistical analysis

All statistical analyses were performed using SPSS version 25 (IBM Corp., Armonk, NY). The Kolmogorov-Smirnov test was employed to determine distribution. Qualitative variables were described as frequencies and percentages. Quantitative variables were measured by mean (SD, standard deviation) and median (IQR, interquartile range), as appropriate. The differences between groups were analyzed by the *t*-test and the Mann-Whitney *U* test, as appropriate. The Chi-squared test was performed to differentiate ultrasound findings between groups. A *p*-value < 0.05 was considered statically significant.

Results

Fifty-six patients with RA consented and enrolled in the study, 28 were diagnosed with RCT, and 28 were in the comparative group. Socio-demographic and clinical characteristics are summarized in Table 1. Most of the patients were female (96%) with a mean age of 53 ± 12.8 years. The median (IQR) disease duration was 8 (3-11) years. Twenty-three (41%) patients had high blood pressure, 10 (18%) had osteoporosis, and 9 (19%) had diabetes, 36 (64%) were treated with glucocorticoids, and 54 (96%) were taking conventional disease-modifying antirheumatic drugs (csDMARDs). Regarding laterality, 15 (53.6%) patients in the RCT group had right shoulder involvement, 8 (28.6%) had left shoulder involvement, and 5 (17.9%) presented bilateral tendinopathy.

Clinimetry and laboratory findings

Comparing RA activity based on DAS 28 CRP patients with RCT had greater mean (SD) scores, 5.23 (1.28) vs. 3.08 (1.22), *p* < 0.001; as well DAS 28 ESR (5.43, SD = 1.28 vs. 3.66, SD = 1.12, *p* < 0.001). Patients with RCT showed higher ESR serum levels than those without RCT, with a median (IQR) of 33.5 mm/H (20.7-39.7) vs. 25 mm/H (21-37). CRP median (IQR) levels differed significantly between the groups, 5 mg/dL (0.63-5) vs. 0.45 mg/dL (0.22-1.98), respectively (*p* = 0.002). Regarding disease severity, CDAI median scores revealed differences between the groups with a higher score in patients with RCT (20.5 vs. 6, *p* < 0.001). The median (IQR) number of tender joints was significantly higher in the RCT group, 8 (4-19.7) vs. 2 (0.25-6), *p* < 0.001, as well as the number of swollen joints, 2 (1-6.7) vs. 0 (0-2), *p* < 0.003.

VAS median scores were significantly higher in the RCT group (7 vs. 2, *p* < 0.001). The HAQ-DI mean score was significantly higher than the group without RCT (1.09 ± 0.51 vs. 0.43 ± 0.38, *p* < 0.001). The DASHe score revealed important statistical differences between the groups; patients in the RCT group had a median (IQR) score of 38.91 (20.2-50.7) compared to the group without RCT, 6.25 (1.88-15.84), (*p* < 0.001). The HAQ-DI mean (SD) score was significantly elevated in the RCT group in contrast to the comparative group, 1.09 (0.51) vs. 0.43 (0.38), *p* < 0.001.

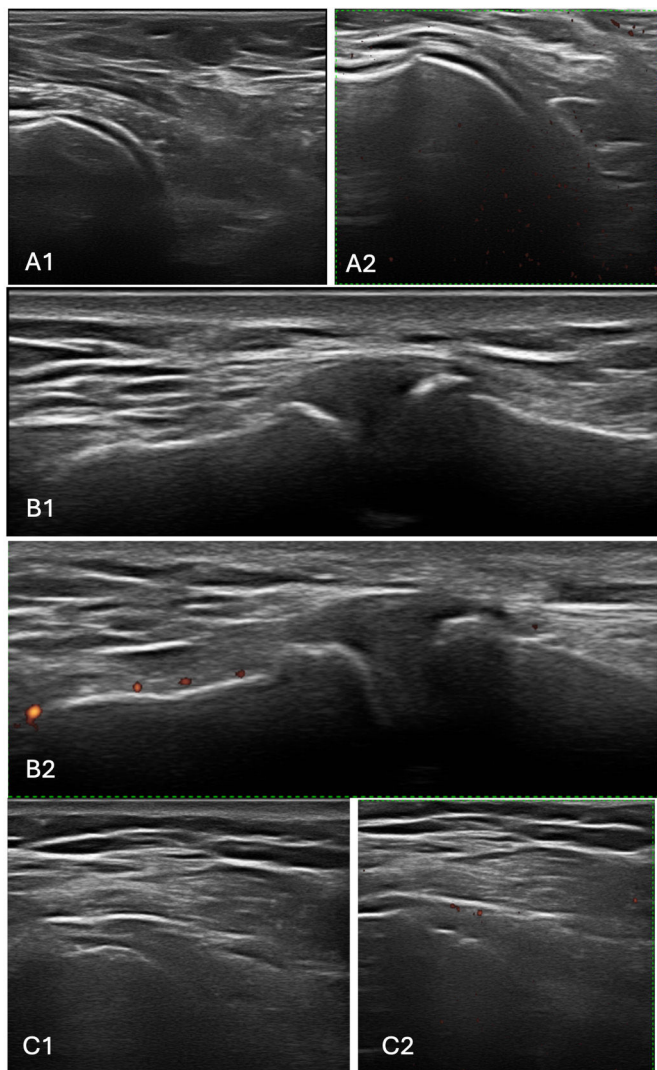


Fig. 2. Ultrasound findings in a patient with rheumatoid arthritis without rotator cuff tendinopathy. Images of the left shoulder showing active synovitis and arthrosis of the acromioclavicular and glenohumeral joints. (A1) Longitudinal grayscale view of the anterior glenohumeral joint. (A2) Corresponding Doppler view. (B1) Grayscale image of the left acromioclavicular joint. (B2) Doppler image of the same region. (C1) Posterior glenohumeral joint in grayscale. (C2) Doppler image of posterior glenohumeral joint.

Ultrasound

Acromioclavicular synovitis was found in 12 (21%) out of 56 patients. Table 2 reports the prevalence of the US findings at the shoulder level between the groups. Acromioclavicular synovitis was found with greyscale ultrasound in 8 (28.6%) patients with RCT and 4 (14.3%) without RCT ($p = 0.193$). Acromioclavicular and glenohumeral arthrosis were more frequently found in the RCT group (60.7% vs. 46.4%); however, this was not statistically significant ($p = 0.33$).

Discussion

Our study demonstrates that RA patients with RCT exhibit significantly higher DAS28 scores, indicating higher RA activity. The presence of RCT in patients with RA without evident synovitis supports the hypothesis that the increase in disease activity, might be influenced by pain unrelated to joint pathology, which may amplify the overall clinical impression.¹⁹ Similar to other

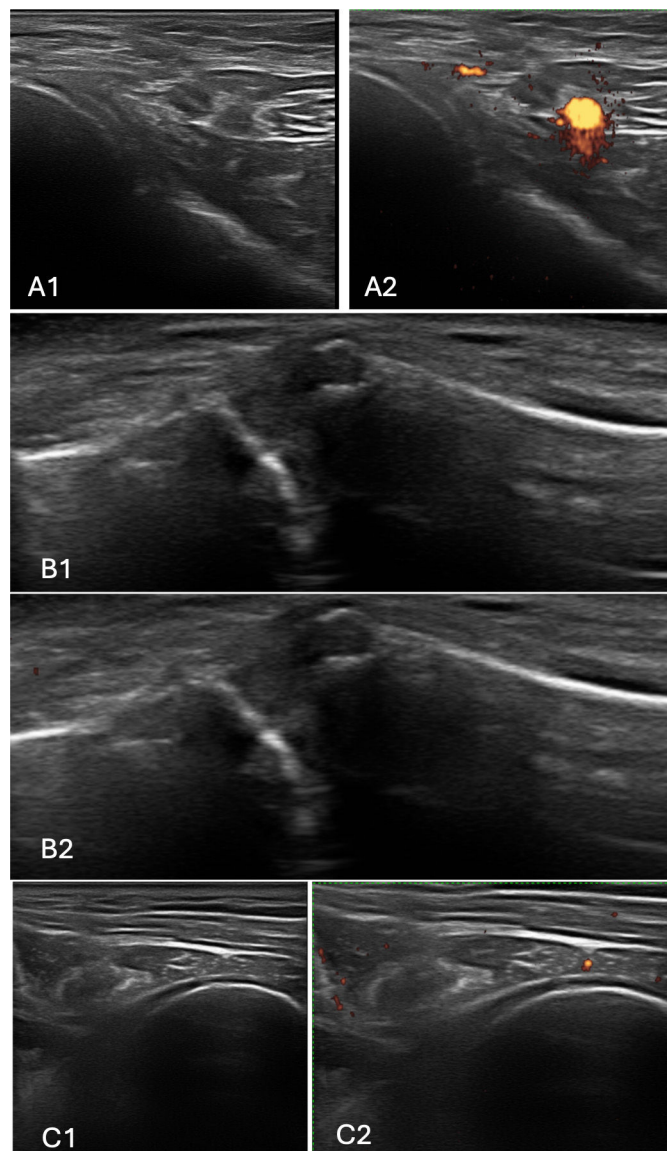


Fig. 3. Ultrasound findings in a patient with rheumatoid arthritis and rotator cuff tendinopathy. Images of the right shoulder showing degenerative changes in the acromioclavicular and glenohumeral joints, with no evidence of synovitis. (A1) Grayscale longitudinal view of the anterior glenohumeral joint. (A2) Corresponding Doppler image. (B1) Grayscale images of the acromioclavicular joint. (B2) Doppler signal of the same region. (C1) Posterior glenohumeral joint in grayscale. (C2) Corresponding Doppler image.

non-inflammatory diseases like fibromyalgia,^{19,20} depression, psychological distress,²⁰ and osteoarthritis,²¹ RCT could also impact disease activity scores.

The shoulder is a common site of MS pain, affecting a median of 16% of the general population,²² with rotator cuff disorders being the leading cause.²³ Patients with RA are at a higher risk of rotator cuff disease, probably due to chronic inflammation and tendon degeneration resulting in weakness of the rotator cuff muscles.⁹ The shoulder joint accounts for 11–27% of clinimetric indexes²⁴ and significantly contributes to general and pain VAS score, as well as HAQ scores.²⁵ Given its impact, results should be interpreted cautiously, considering the specific characteristics of the pain. Since the shoulder is often one of the last joints affected by RA,²⁶ and RCT is multifactorial – combining extrinsic mechanical compression and tendon overuse/overload,^{8,27} other factors should be considered before assuming that RCT is a direct consequence of

Table 1
Patient demographics and treatment.

Characteristic	RA + RCT n = 28	RA + NRCT n = 28	p-Value
Age, mean (SD)	55.04 (10.87)	51.64 (14.51)	0.327 [†]
BMI, mean (SD)	28.25 (5.02)	27.53 (4.22)	0.565 [†]
Disease duration in years, median (IQR)	8 (3.25–13.50)	5 (1.25–10.75)	0.202 [‡]
Sex, n (%)			0.245 [§]
Women	28 (100)	26 (92.8)	
Men	0 (0)	2 (7.14)	
Disease activity, n (%)			0.001 [§]
High activity	14 (50)	2 (7.14)	
Moderate activity	14 (50)	16 (57.14)	
Mild activity	0	4 (14.28)	
Remission	0	6 (21.42)	
Painkillers, n (%)	9 (32)	6 (21)	0.365 [†]
Glucocorticoids, n (%)	20 (72)	16 (57)	0.265 [†]
DMARDs, n (%)	27 (96)	27 (96)	–

RA + RCT, rheumatoid arthritis + rotator cuff tendinopathy; RA + NRCT, rheumatoid arthritis + no rotator cuff tendinopathy; BMI, body mass index; SD: standard deviation; IQR: interquartile range; DMARDs, disease-modifying antirheumatic drugs.

[†] Student's *t* test.

[‡] Mann–Whitney *U* test.

[§] Chi-square test.

Table 2
Clinimetry and clinical characteristics.

Characteristic	RA + RCT n = 28	RA + NRCT n = 28	p-Value
ESR*, median (IQR)	33.50 (20.75–39.75)	25.00 (21.00–37.00)	0.290 [†]
CRP**, median (IQR)	5.00 (0.63–5.00)	0.45 (0.22–1.98)	0.002[‡]
VAS, median (IQR)	70.00 (52.50–80.00)	20.00 (12.50–40.00)	<0.001[‡]
HAQ-DI, mean (SD)	1.09 (0.51)	0.43 (0.38)	<0.001[‡]
CDAI, median (IQR)	20.50 (12.50–35.00)	6.00 (2.00–13.75)	<0.001[‡]
DASH, median (IQR)	38.91 (20.20–50.79)	6.25 (1.88–15.84)	<0.001[‡]
DAS28 CRP, mean (SD)	5.23 (1.28)	3.08 (1.22)	<0.001[‡]
DAS28 ESR, mean (SD)	5.43 (1.28)	3.66 (1.12)	<0.001[‡]
Ultrasound, n (%)			0.193 [§]
Without synovitis ^{††}	20 (71.4)	24 (85.7)	
Acromioclavicular synovitis ^{††}	8 (28.6)	4 (14.3)	
Glenohumeral synovitis ^{††}	0 (0)	0 (0)	
Ultrasound, n (%)			0.33 [§]
Without arthrosis ^{††}	1 (3.6)	3 (10.7)	
Acromioclavicular arthrosis ^{††}	1 (3.6)	4 (14.3)	
Glenohumeral arthrosis ^{††}	9 (32.1)	8 (28.6)	
Acromioclavicular arthrosis and glenohumeral arthrosis ^{††}	17 (60.7)	13 (46.4)	

RA + RCT, rheumatoid arthritis + rotator cuff tendinopathy; RA + NRCT, rheumatoid arthritis + No rotator cuff tendinopathy; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein; VAS, visual analog scale; HAQ-DI, Health Assessment Questionnaire-disability index; CDAI, Clinical Disease Activity Index; DASH, Disabilities of the Arm, Shoulder, and Hand Questionnaire; DAS 28 CRP, Disease Activity Score 28 C-reactive protein; DAS 28 ESR, Disease Activity Score 28 erythrocyte sedimentation rate; SD: standard deviation, IQR: interquartile range.

* mm/H.

** mg/dL.

[†] Student's *t* test.

[‡] Mann–Whitney *U* test.

[§] Chi-square test.

^{††} n (%). Bold values are statistically significant.

RA. This is also supported by the absence of significant difference among groups when comparing ultrasound signs attributed to RA activity.

The differences in disease activity scores between RA patients with and without RCT highlight the impact on disease perception and management. All patients with RCT exhibited moderate to high disease activity, since the severity of the disease is one of the leading indicators of functional capacity,²⁸ it can be compromised by RCT, as reflected in the HAQ-DI scores.

In contrast, only 2 patients without RCT had high disease activity, and just over half had moderate activity. The rest presented mild activity or were in remission. Probably explained by the fluctuation of symptoms over time and the dynamic nature of RA.

The manage of care in RA follows a treat-to-target approach, requiring regular assessment of disease activity.²⁹ However, if judgments are made solely on DAS28, patients may receive inadequate medical care for their specific disorder, as DAS28 is a supportive tool that represents patient's disease activity but may not fully capture the complexity of an individual patient's clinical presentation. Given this and considering the impact of RCT in RA disease activity scores, an intentional examination of the shoulder is essential when patients complain of shoulder pain and limited range of motion.

As the management of RA and RCT differs, it is necessary to treat RCT specifically. Although painkillers and steroids can alleviate the pain associated with both conditions, RCT requires its

own treatment such as active exercise, physical therapy, corticosteroid injections, or even a surgical intervention.⁹ These address the underlying tendon issues directly, unlike RA treatments which focus on reducing inflammation and immune system activity. By specifically treating RCT, we can improve the accuracy in the assessment of RA disease activity and improve the scores.

Our study has some limitations. Given the cross-sectional nature of the study, by the time of ultrasound performance, patients did not have synovitis which could have led to tendinopathy and shoulder pain. Besides, markers such as VAS, the number of swollen joints, and the number of painful joints are dynamic and can change over time. It is possible that the tendinopathy detected during the evaluation may result from previous elevated disease activity, including synovitis in the subacromial space which was not detected at the time of the study. Another limitation is that the ultrasound assessments were conducted by a single operator.

We emphasize that at the time of evaluation, patients did not have synovitis in joints that could lead to shoulder pain. Even though DAS28 score majorly depends on acute reactants factors, we found a significant difference of more than 50 mm in VAS between the RCT group and those without it; consistent with the pain contribution of shoulder involvement.²⁷ It is beyond the scope of this study to determine which clinical feature is most responsible for the elevation of the disease activity score; however, it is recommended that further research be undertaken to investigate the relationship between RCT and high disease activity in RA more thoroughly.

Conclusion

RA patients with RCT have higher composite index and disease activity scores than those without RCT. An intentional screening for RCT should be recommended for those patients with shoulder pain and elevated disease activity to achieve optimal patient-tailored care and appropriate treatment management.

Author contributions

All authors contributed to the study's conception and design. Material preparation was performed by JMC, JAEV, DVM, RJCDLG, and LDLCB. RJCDLG and AADLP did the formal analysis and investigation. JMC collected the data. RJCDLG, AEMM, and LGF wrote and prepared the original draft. Review and editing were performed by RJCDLG, DVM, AALP, and LGF. All authors commented on previous versions of the manuscript, read and approved the final manuscript. All authors take full responsibility for the integrity and accuracy of all aspects of the work.

Compliance with ethical standards

Study was performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments. All patients gave their individual informed consent for processed data and publication before their inclusion in this study. The protocol was approved by the Institutional Ethics and Research Committee (RE22-00001). Patients were aware of what kind of personal data was processed, how would it be used and for which purpose.

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Conflict of interest

All the authors in this paper declare no conflict of interest.

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