Original Article

Ultrasonographic Evaluation of the Ankle Joint in Relation to Rheumatoid Factor Status and Disease Activity in Patients with Rheumatoid Arthritis

Adel Ibrahim Azzam*

Department of Rheumatology and Rehabilitation, Faculty of Medicine, Al-Azhar University, Cairo, Egypt

Abstract

Background: Rheumatoid arthritis (RA) is a form of inflammatory disease whose clinical pattern is largely dependent on the presence of both anti-citrullinated protein antibodies and rheumatoid factor (RF). Although this is still debatable, seronegative RA seems to be a somewhat less serious condition. The present study aimed to evaluate ankle joint ultrasound in relation to RF status and disease activity in RA patients. **Methods:** A cross-sectional study involving RA patients from a single center was conducted. Laboratory test evaluations and clinical activity assessments were carried out. The ankle joint was examined using musculoskeletal ultrasound (US). **Results:** The study included 100 patients with established RA in total. Eighty-two patients tested positive for RF with a mean age of 42.3, whereas only 18 tested negative with a mean age of 39.6. Patients who tested positive for RF had a longer duration of illness (9.39 ± 5.39 vs. 4.56 ± 3.24). There were no differences in clinical activity scores between the seropositive and seronegative groups. The pathological US findings of any ankle joint showed no differences between the seropositive and seronegative groups. Patients with US findings of tibialis posterior tenosynovitis in the left ankle and synovitis and erosion in the right ankle, particularly in the tibiotalar and talonavicular joints, had significantly high Disease Activity Score 28-Erythrocyte sedimentation rate-scores. The increased disease activity was accompanied by significant erosions on both ankles. **Conclusion:** In terms of disease activity, there is no clinically significant difference between seropositive and seronegative RA patients. Sonographic ankle joint abnormalities do not appear to be associated with the patients' RF status. High RA disease activity, on the other hand, is associated with synovitis and erosions, particularly in the talonavicular and tibiotalar joints, as well as tibialis posterior tenosynovitis.

Keywords: Ankle joint, rheumatoid arthritis, rheumatoid factor, seronegative rheumatoid arthritis, ultrasound

Introduction

Rheumatoid arthritis (RA) is a systemic inflammatory disorder that primarily affects the synovial joints of the hand and foot, resulting in cartilage and bone destruction.[1] Foot or ankle involvement occurs early in the disease course in approximately 90% of patients. Of them, 20% first developed foot or ankle arthritis.[2]

To classify RA, anti-citrullinated protein antibodies (ACPAs) and rheumatoid factor (RF) serology are used. The clinical course and presentation of seronegative RA appear to be less severe than those of seropositive RA, yet there are still disagreements because other research has not found these differences.[3]

Using Ultrasound (US) examination can assist in the diagnosis of conditions that go undetected clinically. Furthermore, US can aid in the identification of synovitis, bone erosions, and tenosynovitis, all of which are clues for diagnosis and effective treatment plans.[4] Furthermore, in a variety of disorders, including shoulder impingement syndrome, the US may display dynamic changes in real time.[5] In addition, it is safe to provide corticosteroid or other therapeutic injections for joints, bursae, or tendon sheaths under sonographic guidance.[6]

A normal gait depends on an ankle joint that is functioning properly.[7] It is crucial to recognize ankle problems in patients

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Address for correspondence: Prof. Adel Ibrahim Azzam, Department of Rheumatology and Rehabilitation, Faculty of Medicine, Al-Azhar University, Cairo, Egypt.
E-mail: adelazzam25@yahoo.com

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with RA so that therapy may be started promptly to prevent worsening.[8] When ankle discomfort is present, US is a reliable method of imaging that enables the identification of the damaged anatomic structures, elucidating their origin, and identifying subclinical ankle disorders.[9]

According to earlier studies, many clinical and sonographic ratings utilized for the diagnosis and follow-up of RA patients disregard the examination of the ankle joint. The usefulness of ankle joint assessment in RA and the evaluation of ultrasonographic data based on the frequency, duration, and activity of the disease need to be determined with greater diligence.[10]

Given the scarcity of studies assessing and correlating ankle joint US findings with disease activity or RF status, we decided to conduct a detailed US examination of the ankle joint in RA patients and compare disease activity, disease duration, and RF status with the ankle sonographic findings.

Methods

Design

This was a single-center cross-sectional study, which was approved by the ethical committee of the Al-Azhar Faculty of Medicine with acceptance number 0000052 by the ethics board of the university. All participants gave written informed consent before participating in the trial. It adheres to the legal principles set forth in the Helsinki Declaration. Each medical file comprising all inquiries had a code number, ensuring the confidentiality of all patient information.

Participants

Patients with RA were recruited from the inpatient and outpatient clinics of the Rheumatology and Rehabilitation Department. A total of 145 RA patients were evaluated, with 100 eventually enrolled and 45 failing to meet the inclusion criteria. Figure 1 shows the study's flow diagram.

Patients had to be over the age of 18 years and meet the European League Against Rheumatism/American College of Rheumatology (EULAR/ACR 2010) criteria for RA diagnosis to be included in the research.[11] The presence of synovitis in at least one joint, the absence of a diagnosis that more adequately explains the synovitis, and the achievement of a total score of at least 6 (out of a possible 10) from the individual scores in four domains constitute the diagnosis of definite RA, according to the 2010 ACR/EULAR classification criteria for RA. The highest score attained in a certain domain is used in this calculation. All patients underwent history-taking and a clinical examination. Patients were considered symptomatic if they felt pain in the ankle joint. The Disease Activity Score 28-Erythrocyte sedimentation rate (DAS28-ESR) was used to evaluate RA activity.[12]

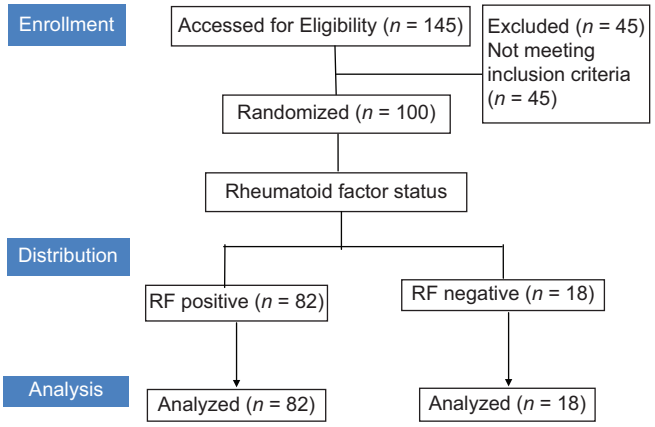

Figure 1: Flow chart of the study subjects. RF: Rheumatoid factor

Patients under the age of 18 years, those with diabetes or hepatitis C virus infection, those who were pregnant, those with overlap with other connective-tissue diseases, those who had prior surgery on the ankle or trauma, and those who got their ankles injected were all eliminated.

Ankle ultrasound

The linear probe Philips Affiniti 50 G (Philips Healthcare, Andover, United States) was used for the US assessment. The tibiotalar and talonavicular joints (TNJ) were examined for synovitis and/or effusion in grayscale (GS) and power Doppler (PD). Fluid distension >3 mm in the tibiotalar joint (TTJ) and >2.6 mm in the TNJ was defined as effusion.[13]

The patients were lying down with their knees bent to 45° and their soles facing the bed. The anterior medial and lateral compartments of the TTJ were studied, whereas the TNJ was evaluated just from its anterior aspect. On GS and PD, the extensor tendons, comprising the tibialis anterior, extensor hallucis longus, and extensor digitorum longus, were tested for tenosynovitis and/or tendinosis. The tibialis posterior, flexor digitorum, and flexor hallucis longus were also tested on the medial side. The peroneus longus and brevis tendons on the lateral side were studied using the same standards.[14,15]

Starting with the myotendinous junction in the sagittal and axial planes, all tendons were inspected over their entire length. Static and dynamic analyses were also performed.[14] Tendinosis was characterized as tendon enlargement with disruption of the typical fibrillar architecture and hypoechogenicity.[16] Erosion was visible in both the longitudinal and transverse planes, with substantial loss of bone cortex.[17] Synovitis was characterized as either a hypoechoic or anechoic intra-articular compressible structure without a Doppler signal (effusion) or an aberrant intra-articular hypoechoic non or weakly compressible tissue with a Doppler signal (synovial proliferation).[18] According to Alcalde *et al*.,[19] tenosynovitis is described as hypo- or anechoic tissue swelling that includes fluid within the tendon sheath and can be visible in two perpendicular planes with or without a Doppler signal. A semiquantitative technique (grade 0–3) by PD was used to determine the degree of synovitis and synovial/tenosynovial vascularity. A semiquantitative GS evaluation of synovitis (effusion and/or synovial hypertrophy) was conducted.[20] According to Ohrndorf *et al*.,[21] tenosynovitis and erosion in GS were rated as 0 when missing or 1 when present.

All the trial participants were receiving disease-modifying antirheumatic drugs (DMARDs) and had no prior experience with biological therapy.

An experienced rheumatologist (AIA) with around 9 years of musculoskeletal ultrasonography expertise examined both ankles of each patient on the same day as the clinical evaluation. The same individual used a Philips Affiniti 50 G (Philips Healthcare, Andover, United States) with a 13 MHz superficial probe to scan each patient.

Analysis

The Statistical Package for the Social Sciences (SPSS, IBM Inc., Armonk, NY, USA) version 26 for Windows was used to introduce and statistically analyze the obtained data. Numbers and percentages were used to define qualitative data. As necessary, the Fisher's exact test and the Chi-square test were utilized to compare categorical variables. The Kolmogorov–Smirnov test was used to determine if quantitative data were normal. The mean and standard deviation of the variables were used to define their normal distribution, and an independent sample *t*-test was employed to compare the characteristics of the groups. A statistically significant *P* value was ≤0.05.

Results

The current study comprised 100 patients with established RA who were classified based on their RF state [Table 1]. There were 82 seropositive RA patients (91.5% female) and 18 seronegative RA patients (100% female). The mean age of the seropositive group was 42.3 ± 11.6, whereas the seronegative group was 39.6 ± 7.4. There was no statistically significant difference in age, gender, or body mass index (BMI) between individuals with positive or negative RF.

We also found no statistically significant difference between the two groups in terms of the degree of RA disease activity as indicated by the DAS28-ESR score. Rheumatoid patients with seropositive status had a considerably longer illness duration than those with seronegative status, although there was no significant difference in ankle joint symptomatology in both groups [Table 2].

In terms of GS and PD US findings in the two groups, our findings showed that the most common pathologies detected by GS and PD US in the anterior compartment of the right ankle were synovitis (synovial effusion or hypertrophy) of the tibiotalar and TNJ, followed by tenosynovitis of the tibialis anterior tendon. There was no significant difference in GS or PD results between individuals with seropositive or seronegative RA [Table 3].

We also identified no significant difference in GS or PD between the two groups of the medial, lateral, and posterior compartments of the right ankle [Table 4].

Regarding the left ankle joint, we found that there was virtually no difference between the RF positive and negative groups in any compartment assessed by GS and PD scan [Tables 5 and 6].

Table 1: Demographics of patients with positive or negative rheumatoid factor

	Positive RF (*n*=82)	Negative RF (*n*=18)	*P*
Age (years)			
Mean±SD	42.3±11.6	39.6±7.4	0.224
Range	20–60	25–54	
Gender, *n* (%)			
Male	7 (8.5)	0	0.345
Female	75 (91.5)	18 (100)	
BMI (kg/m^2)			
Mean±SD	28.5±5.4	27±3.8	0.284
Range	15.2–47.9	22.4–35.9	

RF: Rheumatoid factor, SD: Standard deviation, BMI: Body mass index

Table 2: Disease characteristics of patients with positive or negative rheumatoid factor

	Positive RF (*n*=82)	Negative RF (*n*=18)	*P*
DAS28-ESR			
Mean±SD	4.66±1.14	4.67±1.23	0.921
Range	2.55–6.96	2.8–6.8	
DAS28-ESR categories, *n* (%)			
Low	11 (13.4)	4 (22.2)	0.754
Moderate	29 (35.4)	6 (33.3)	
High	41 (50)	8 (44.4)	
Remission	1 (1.2)	0	
ESR (mm/h)			
Mean±SD	43.8±17.9	37.3±14.3	0.153
Range	14–105	24–80	
Disease duration (years)			
Mean±SD	9.39±5.39	4.56±3.24	<0.001*
Range	3–25	3–16	
Symptoms, *n* (%)			
No symptoms	28 (34.1)	10 (55.6)	0.057
Right ankle	9 (11)	0	
Left ankle	11 (13.4)	4 (22.2)	
Bilateral	34 (41.5)	4 (22.2)	

*Statistically significant as *P*≤0.05. DAS: Disease activity score, ESR: Erythrocyte sedimentation rate, RF: Rheumatoid factor, SD: Standard deviation

When we classified our patients based on their DAS28-ESR scores, we discovered that GS synovitis (synovial hypertrophy) of both the TTJ and the TNJ in the right ankle, as well as tibialis posterior tenosynovitis in the left ankle, were more substantial in patients with high disease activity compared to those with low or moderate disease activity [Tables 7 and 8]. The remaining GS and PD US data in all compartments revealed no statistically significant differences between individuals with different DAS28-ESR grades [Supplementary Tables 1 and 2].

In both ankles, individuals with moderate and high disease activity levels had substantially more bone erosions than patients with low disease activity, as determined by DAS28-ESR [Table 9]. The pathologies of some of the study participants are depicted in Figure 2.

Table 3: Right ankle joint anterior compartment of patients with positive or negative rheumatoid factor

	Positive RF (*n*=82), *n* (%)	Negative RF (*n*=18), *n* (%)	*P*
GS US			
TTJ			
Synovial effusion	8 (9.8)	1 (5.6)	1.000
Synovial hypertrophy	26 (31.7)	3 (16.7)	0.203
TNJ			
Synovial effusion	2 (2.4)	0	1.000
Synovial hypertrophy	17 (20.7)	6 (33.3)	0.352
Anterior ankle. Tenosynovitis			
TA	20 (24.4)	1 (5.6)	0.110
EHL	1 (1.2)	1 (5.6)	0.329
EDL	3 (3.7)	2 (11.1)	0.219
PD US			
TTJ			
Grade 1	2 (2.4)	0	1.000
TNJ			
Grade 1	1 (1.2)	0	1.000
TA			
Grade 1	3 (3.7)	0	1.000
Bone erosion	3 (16.7)	31 (37.8)	0.086

GS: Grayscale, PD: Power Doppler, TTJ: Tibiotalar joint, TNJ: Talonavicular joint, TA: Tibialis anterior tendon, EHL: Extensor hallucis longus tendon, EDL: Extensor digitorum longus tendon, RF: Rheumatoid factor, US: Ultrasound

Table 4: Right ankle joint medial, lateral, and posterior compartments of patients with positive or negative rheumatoid factor

	Positive RF (*n*=82)	Negative RF (*n*=18)	*P*
GS US			
Medial ankle. Tenosynovitis			
TP	55 (67.1)	9 (50)	0.172
FDL	8 (9.8)	5 (27.8)	0.055
FHL	0	0	-
Lateral ankle. Tenosynovitis			
PL	32 (39)	5 (29.4)	0.456
PB	32 (39)	5 (27.8)	0.371
Posterior ankle			
ATE	6 (7.3)	0	0.588
ATB	0	0	-
PD US			
TP			
Grade 1	6 (7.3)	1 (5.6)	0.640
Grade 2	2 (2.4)	0	
FDL			
Grade 1	1 (1.2)	1 (5.6)	0.329
PL			
Grade 1	9 (11)	3 (16.7)	0.668
Grade 2	2 (2.4)	0	
Grade 3	1 (1.2)	0	
PB			
Grade 1	8 (9.8)	3 (16.7)	0.538
Grade 2	3 (3.7)	0	
Grade 3	1 (1.2)	0	
ATE			
Grade 2	1 (1.2)	0	1.000

GS: Grayscale, PD: Power Doppler, TP: Tibialis posterior, FDL: Flexor digitorum longus tendon, FHL: Flexor hallucis longus tendon, PL: Peroneus longus tendon, PB: Peroneus brevis tendon, ATE: Achilles tendon enthesopathy, ATB: Achilles tendon bursitis, RF: Rheumatoid factor, US: Ultrasound

Discussion

It is still unknown whether seropositive RA patients experience a worse disease course in terms of disease activity and radiological results than seronegative patients. It has been reported that individuals with seropositive RA had worse disease symptoms and function both at the time of diagnosis and after receiving DMARD therapy.[22] Although there is still disagreement, seronegative RA is thought to be a less severe illness than seropositive RA.[23] The purpose of this study was to determine if there was an association between ankle joint sonographic findings and disease activity and RF status in RA patients.

In this research, despite no changes in age, gender, or BMI between both groups, we observed substantial differences in RA disease duration as the seropositive individuals had a longer course of the disease (9.39 ± 5.39 years) compared to seronegative patients (4.56 ± 3.24 years). Carbonell-Bobadilla *et al*.[3] reported that seropositive RA patients had a younger age at disease onset than seronegative patients (43 ± 14 vs. 54 ± 11; $P = 0.00$).

Confirming our results, Carbonell-Bobadilla *et al*.[3] reported that there were no differences in clinical activity between RA patients with seropositive and seronegative RF status.

Our results differ from those presented by Mouterde *et al*.[24] and Choi and Lee.[25] In the study of Mouterde *et al*.,[24] an initial cohort of patients with early inflammatory arthritis was intended to highlight the clinical history of individuals lacking RF and ACPA and identify preliminary determinants of achieving 2010 ACR/EULAR criteria for RA over a 3-year period. They stated that in comparison to seropositive patients, seronegative individuals had less disease activity as measured by DAS28-ESR and less severity as measured by the functional scale and radiological scores at baseline.

On the other hand, it was reported that patients with RA who were seronegative at baseline showed an even more severe disease than RA patients who were seropositive.[25] The fact that just 27.5% of seronegative patients with RA matched the 2010 ACR/EULAR criteria, compared to 99.5% of seropositive RA patients, may help to explain this. The 2010 ACR/EULAR criteria place a lot of emphasis on serology indicators to identify patients with RA early in the course of the illness. As a result, RA might be identified in seropositive individuals who only had one or two affected joints.[26] This may account for

Table 5: Left ankle joint anterior compartment of patients with positive or negative rheumatoid factor

	Positive RF (n=82), n (%)	Negative RF (n=18), n (%)	P
GS US			
TTJ			
Synovial effusion	2 (2.4)	0	1.000
Synovial hypertrophy	13 (15.9)	1 (5.6)	0.455
TNJ			
Synovial effusion	5 (6.1)	0	0.582
Synovial hypertrophy	23 (28)	5 (27.8)	1.000
Anterior ankle. Tenosynovitis			
TA	9 (11)	0	0.357
EHL	2 (2.4)	0	1.000
EDL	1 (1.2)	0	1.000
PD US			
TTJ			
Grade 1	3 (3.7)	1 (5.6)	0.554
TA			
Grade 1	2 (2.4)	0	1.000
Bone erosion	4 (22.2)	24 (29.3)	0.547

GS: Grayscale, PD: Power Doppler, TTJ: Tibiotalar joint, TNJ: Talonavicular joint, TA: Tibialis anterior tendon, EHL: Extensor hallucis longus tendon, EDL: Extensor digitorum longus tendon, RF: Rheumatoid factor, US: Ultrasound

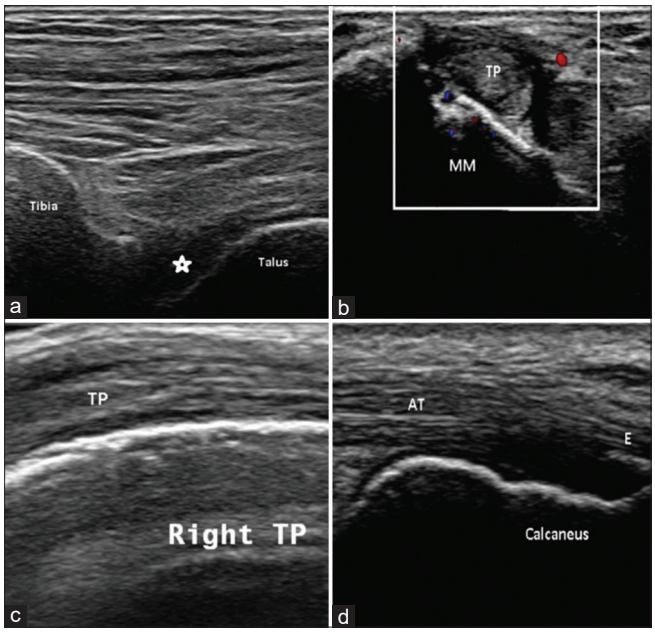

Figure 2: (a) Anterior longitudinal scan of the ankle joint demonstrating a synovitis-related hypoechoic lesion (asterisk) in the tibiotalar recess. (b and c) A scan of the tibialis posterior tendon at the medial malleolus reveals a positive Doppler signal in the transverse (b) and longitudinal (c) scans, indicating active tenosynovitis. (d) An anterior longitudinal scan of the achilles tendon over the calcaneus reveals a formation of enthesophytes and the loss of the tendon's typical fibrillar echo pattern, both of which indicate achilles enthesitis. TP: Tibialis posterior, AT: Achilles tendon, E: Enthesophyte, MM: Medial malleolus

the longer illness duration in the seropositive RA group that was seen in our research.

Table 6: Left ankle joint medial, lateral, and posterior compartments of patients with positive or negative rheumatoid factor

	Positive RF (n=82), n (%)	Negative RF (n=18), n (%)	P
GS US			
Medial ankle. Tenosynovitis			
TP	51 (37.8)	14 (77.8)	0.209
FDL	5 (6.1)	2 (11.1)	0.606
FHL	1 (1.2)	0	1.000
Lateral ankle. Tenosynovitis			
PL	26 (31.7)	6 (33.3)	0.893
PB	24 (29.3)	6 (33.3)	0.733
Posterior ankle			
ATE	8 (9.8)	0	0.344
ATB	0	0	-
PD US			
TP			
Grade 1	5 (6.1)	4 (22.2)	0.064
Grade 2	5 (6.1)	0	
FDL			
Grade 1	1 (1.2)	0	1.000
PL			
Grade 1	9 (11)	3 (16.7)	0.635
Grade 2	2 (2.4)	1 (5.6)	
PB			
Grade 1	8 (9.8)	3 (16.7)	0.524
Grade 2	2 (2.4)	1 (5.6)	
ATE			
Grade 2	1 (1.2)	0	1.000

GS: Grayscale, PD: Power Doppler, TP: Tibialis posterior tendon, FDL: Flexor digitorum longus tendon, FHL: Flexor hallucis longus tendon, PL: Peroneus longus tendon, PB: Peroneus brevis tendon, ATE: Achilles tendon enthesopathy, ATB: Achilles tendon bursitis, RF: Rheumatoid factor, US: Ultrasound

It has been suggested that seronegative RA is believed to be a less severe illness with less radiographic destruction than seropositive RA.[27] Considering this, it has been proposed that seronegative individuals should get less intense therapy than seropositive patients, which is further stated in the 2016 EULAR recommendations for treatment.[28]

According to Nordberg *et al.*'s[29] research, seronegative RA is not a minor variant of the illness and needs intense treat-to-target treatment identical to that given to seropositive RA patients. In this investigation, there was a tendency toward higher radiographic destruction in seronegative individuals as opposed to seropositive patients, both at the beginning and after a period of 24 months. Seropositive patients had a greater treatment response at 3 months than seronegative patients, although both groups had equal numbers of patients in remission at the conclusion of the research. This finding would suggest that seronegative individuals may benefit from treat-to-target approaches, even if their initial response to therapy is slower than that of seropositive patients.

Table 7: Right ankle joint anterior compartment of studied patients with different disease activity score 28 grades

	Low (*n*=15), *n* (%)	Moderate (*n*=35), *n* (%)	High (*n*=49), *n* (%)	*P*
GS US				
TTJ				
Synovial effusion	0	3 (8.6)	6 (12.2)	0.350
Synovial hypertrophy	0[a]	9 (25.7)[a,b]	20 (40.8)[b]	0.008*
TNJ				
Synovial effusion	0	2 (5.7)	0	0.120
Synovial hypertrophy	0[a]	7 (20)[a,b]	16 (32.7)[b]	0.006*
Anterior ankle. Tenosynovitis				
TA	3 (20)	8 (22.9)	10 (20.4)	0.957
EHL	0	0	2 (4.1)	0.240
EDL	0	0	5 (10.2)	0.068
PD US				
TTJ				
Grade 1	0	1 (2.9)	1 (2)	0.697
TNJ				
Grade 1	0	0	1 (2)	0.492
TA				
Grade 1	0	1 (2.9)	2 (4.1)	0.579

*Statistically significant as $P \leq 0.05$. Different superscript letters show significant difference between groups. GS: Grayscale, PD: Power Doppler, TTJ: Tibiotalar joint, TNJ: Talonavicular joint, TA: Tibialis anterior tendon, EHL: Extensor hallucis longus tendon, EDL: Extensor digitorum longus tendon

Table 8: Left ankle joint medial, lateral, and posterior compartments of studied patients with different disease activity score 28 grades

	Low (*n*=15)	Moderate (*n*=35)	High (*n*=49)	*P*
GS US				
Medial ankle. Tenosynovitis				
TP	5 (33.3)[a]	21 (60)[a,b]	38 (77.6)[b]	0.006*
FDL	2 (13.3)	2 (5.7)	3 (6.1)	0.638
FHL	0	0	1 (2)	0.492
Lateral ankle. Tenosynovitis				
PL	2 (13.3)	11 (31.4)	19 (38.8)	0.181
PB	1 (6.7)	11 (31.4)	18 (36.7)	0.084
Posterior ankle				
ATE	0	1 (2.9)	7 (14.3)	0.076
ATB	0	0	0	-
PD US				
TP				
Grade 1	0	3 (8.6)	6 (12.2)	0.096
Grade 2	0	0	5 (10.2)	
FDL				
Grade 1	0	0	1 (2)	0.492
PL				
Grade 1	2 (13.3)	3 (8.6)	7 (14.3)	0.271
Grade 2	0	0	3 (6.1)	
PB				
Grade 1	1 (6.7)	3 (8.6)	7 (14.3)	0.230
Grade 2	0	0	3 (6.1)	
ATE				
Grade 2	0	0	1 (2)	0.492

*Statistically significant as $P \leq 0.05$. Different superscript letters show significant difference between groups. GS: Grayscale, PD: Power Doppler, TP: Tibialis posterior tendon, FDL: Flexor digitorum longus tendon, FHL: Flexor hallucis longus tendon, PL: Peroneus longus tendon, PB: Peroneus brevis tendon, ATE: Achilles tendon enthesopathy, ATB: Achilles tendon bursitis

Table 9: Left and right ankle cortical erosion in patients with different disease activity score 28 grades

	Low (*n*=15)	Moderate (*n*=35)	High (*n*=49)	*P*
Right ankle erosion	1 (6.7)[a]	14 (40)[b]	19 (38.8)[b]	0.049*
Left ankle erosion	0[a]	12 (34.3)[b]	16 (32.7)[b]	0.03*

*Statistically significant as $P \leq 0.05$. Different superscript letters show significant difference between groups

In the present study, the US findings revealed no significant differences in GS or PD at the ankle joint level between seropositive and seronegative RA individuals.

Numerous studies utilizing various US scores found that seropositive RA patients had a higher incidence of damage as determined by GS and PD US. Our findings contradict the findings of Suzuki *et al*.,[30] who found a link between tenosynovitis of the ankle and RF seropositivity. Furthermore, our results were not in line with earlier findings indicating that there is a positive correlation between RF status and erosion.[31]

On the other hand, ACPA status has been linked to a variety of US findings, including proliferative synovitis and a higher percentage of erosions, which were more common in ACPA-positive patients than in ACPA-negative patients.[32]

The discrepancy between our results and those described in previous studies could be explained by the fact that we did not use a larger US score that included several joints and instead relied solely on one joint, which has the disadvantage of not being associated with the highest frequency of synovitis or erosions reported in other joints.

The current study showed that the GS US findings of the ankle joint (tibiotalar and talonavicular synovitis and/or erosions) and tibialis posterior tenosynovitis were associated with high disease activity assessed by DAS28-ESR.

In accordance with our results, Ohrndorf *et al*.[33] reported that synovitis, tenosynovitis, and erosion were all associated with RA disease activity as measured by the DAS28 score.

Finally, our study has some limitations. One of the major limitations is that we did not use a multiple-joint US score, which could have a much higher sensitivity for detecting a high degree of synovitis and erosions. Another limitation was that radiographic evaluation of erosions was not included. The last limitation was that we did not conduct ACPA testing for RA patients, which, if done, could impact the results.

Conclusion

Ultrasound can quickly and precisely identify people with RA who have ankle involvement. Clinicians should be encouraged to use US more frequently to detect pathological ankle issues. Our findings suggest that seropositive RA patients have a longer course of the disease. The ankle joint sonographic outcomes are totally unrelated to RF status. However, the US ankle joint features of GS synovitis, tenosynovitis, and erosions were significantly associated with high disease activity assessed by DAS28-ESR.

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Conflicts of interest

There are no conflicts of interest.

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Supplementary Table 1: Right ankle joint medial, lateral, and posterior compartments of studied patients with different disease activity score 28 grades

	Low ($n=15$), n (%)	Moderate ($n=35$), n (%)	High ($n=49$), n (%)	P
GS US				
Medial ankle. Tenosynovitis				
TP	7 (46.7)	20 (57.1)	37 (75.5)	0.063
FDL	4 (26.7)	2 (5.7)	7 (14.3)	0.130
FHL	0	0	0	-
Lateral ankle. Tenosynovitis				
PL	4 (26.7)	12 (34.3)	21 (43.8)	0.422
PB	4 (26.7)	12 (34.3)	21 (42.9)	0.471
Posterior ankle				
ATE	0	1 (2.9)	5 (10.2)	0.143
ATB	0	0	0	-
PD US				
TP				
Grade 1	1 (6.7)	2 (5.7)	4 (8.2)	0.541
Grade 2	0	0	2 (4.1)	
FDL				
Grade 1	0	0	2 (4.1)	0.240
PL				
Grade 1	0	3 (8.6)	9 (18.4)	0.218
Grade 2	0	1 (2.9)	1 (2)	
Grade 3	0	0	1 (2)	
PB				
Grade 1	0	3 (8.6)	8 (16.3)	0.250
Grade 2	0	1 (2.9)	2 (4.1)	
Grade 3	0	0	1 (2)	
ATE				
Grade 2	0	0	1 (2)	0.492

GS: Grayscale, PD: Power Doppler, TP: Tibialis posterior tendon, FDL: Flexor digitorum longus tendon, FHL: Flexor hallucis longus tendon, PL: Peroneus longus tendon, PB: Peroneus brevis tendon, ATE: Achilles tendon enthesopathy, ATB: Achilles tendon bursitis, US: Ultrasound

Supplementary Table 2: Left ankle joint anterior compartment of studied patients with different disease activity score 28 grades

	Low ($n=15$), n (%)	Moderate ($n=35$), n (%)	High ($n=49$), n (%)	P
GS US				
TTJ				
Synovial effusion	0	0	2 (4.1)	0.240
Synovial hypertrophy	2 (13.3)	4 (11.4)	8 (16.3)	0.811
TNJ				
Synovial effusion	0	1 (2.9)	4 (8.2)	0.245
Synovial hypertrophy	2 (13.3)	8 (22.9)	18 (36.7)	0.130
Anterior ankle. Tenosynovitis				
TA	3 (20)	0	6 (12.2)	0.062
EHL	0	0	2 (4.1)	0.240
EDL	0	0	1 (2)	0.492
PD US				
TNJ				
Grade 1	0	1 (2.9)	3 (6.1)	0.396
TA				
Grade 1	1 (6.7)	0	1 (2)	0.293

GS: Grayscale, PD: Power Doppler, TTJ: Tibiotalar joint, TNJ: Talonavicular joint, TA: Tibialis anterior tendon, EHL: Extensor hallucis longus tendon, EDL: Extensor digitorum longus tendon, US: Ultrasound