Original paper

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Evaluation of remission in patients with radiographic axial spondyloarthritis using an ultrasonography-based enthesitis score: a cross-sectional study

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Abstract

Introduction: This study aimed to evaluate ultrasonographic entheseal abnormalities in patients with radiographic axial spondyloarthritis (r-axSpA) who were in clinical remission for at least 6 months and receiving either nonsteroidal anti-inflammatory drugs (NSAIDs) or biologic agents.

Material and methods: Seventy-two r-axSpA patients were included, divided into NSAID users (n = 23) and biologic agent users (n = 49). Demographic and clinical data were recorded. Ultrasound assessment was performed bilaterally at 10 entheseal sites using a 7–13 MHz linear probe. Elementary lesions defined by OMERACT – hypoechogenicity, thickening, power Doppler (PD) signal, calcification, enthesophyte, and bone erosion – were evaluated and scored on a scale of 0–3. Inflammation scores included hypoechogenicity, thickening, and PD signal; chronicity scores included bone erosion, enthesophyte, and calcification.

Results: A total of 720 entheseal sites were analyzed. The quadriceps tendon was the most frequently affected site (98.6%), followed by the distal patellar tendon (94.4%), Achilles tendon (70.8%), and plantar fascia (70.8%). Hypoechogenicity, thickening, enthesophyte formation, and bone erosion were the most common abnormalities, while PD signals and calcifications were rare. Nonsteroidal anti-inflammatory drug users showed significantly higher C-reactive protein (CRP) (0.62 ±0.53 vs. 0.41 ±0.27 mg/dl, p = 0.027) and erythrocyte sedimentation rate (ESR) levels (11.91 ±7.72 vs. 7.65 ±5.66 mm/h, p = 0.010) than biologic users, despite similar Axial Spondyloarthritis Disease Activity Score with CRP score. Mean inflammation, tissue damage, and total ultrasound (US) enthesitis scores were 4.85 ±4.37, 6.44 ±4.44, and 11.24 ±8.21, respectively, with no significant difference between treatment groups. Seven biologic-treated, overweight, or obese patients had markedly elevated total US scores (30.43 ±5.83), suggesting persistent entheseal inflammation and structural damage.

Conclusions: Ultrasound-based enthesitis scoring may reveal subclinical disease activity in r-axSpA patients in remission, highlighting the added value of integrating musculoskeletal US into disease monitoring.

Key words: ultrasonography, enthesitis, radiographic axial spondyloarthritis, ultrasonography-based enthesitis score.

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Introduction

Spondyloarthropathies (SpA) consist of diseases with similar clinical, laboratory, and radiological features. Diseases such as ankylosing spondylitis (AS), psoriatic arthritis (PsA), reactive arthritis, and enteropathic arthritis are included in this group. In these diseases, findings such as axial involvement, peripheral joint involvement, dactylitis, enthesitis, and acute anterior uveitis can be observed [1]. Axial SpA is divided into radiographic axial (r-axSpa) and non-radiographic axial SpA; r-axSpa is also known as AS [2].

Enthesitis is inflammation at the attachment sites of ligaments, tendons, aponeurosis, and the joint capsule to the bone and is a characteristic clinical finding in AS [3]. Enthesitis occurs in 30–50% of SpA patients and is associated with more severe disease, higher pain scores, and reduced quality of life [4]. The clinical diagnosis of enthesitis is made by detecting tenderness in the enthesis area on physical examination. However, tenderness in the area of enthesis does not always indicate enthesitis, and absence of tenderness cannot exclude enthesitis [5]. Ultrasound (US) is a more sensitive and specific method in the diagnosis of enthesitis than clinical evaluation. Thickening, hypoechogenicity, enthesophytes, calcification and erosions can be detected in enthesis areas with US, and an increase in blood flow, which is an indicator of inflammation, can be seen with power Doppler (PD) imaging [4].

Nonsteroidal anti-inflammatory drugs (NSAIDs) and biological agents are used in the treatment of SpA. Studies have shown that biological agents are more effective than NSAIDs in the treatment of SpA [6]. The aim of this study was to evaluate entheseal changes by US in patients with r-axSpa who had been in remission for at least 6 months according to the clinician and validated disease activity scales, in the NSAID group and in the biological group.

Material and methods

Study design

This cross-sectional study included patients with r-axSpA who were consecutively admitted to the rheumatology clinics of Adana City Training and Research Hospital and Mersin City Training and Research Hospital between 2022 and 2024.

Eligible patients fulfilled the 2009 Assessment of Spondyloarthritis International Society (ASAS) classification criteria for axSpA and were classified as having r-axSpA based on the presence of definite sacroiliitis on pelvic radiographs according to the 1984 Modified New York criteria.

Patients were required to be older than 18 years. Exclusion criteria included a history of infectious disease lasting more than 3 days within the past 6 months, the presence of any ongoing metabolic disease, a diagnosis of any inflammatory rheumatic disease other than r-axSpA, or a history of trauma to entheseal areas.

Remission was defined based on a composite set of clinical, laboratory, and disease activity criteria. Patients were considered in remission if they reported subjective well-being without complaints attributable to disease activity, exhibited no clinical evidence of enthesitis on detailed physical examination, and had normal inflammatory markers, defined as C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) values within the laboratory reference ranges. Additionally, an Axial Spondyloarthritis Disease Activity Score (ASDAS) of less than 2.1 and a Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) score of less than 4 were required. The remission definition employed in this study corresponds to a low disease activity state rather than strict inactive disease (ASDAS < 1.3), reflecting practical clinical standards in the management of r-axSpA. Only patients meeting all of these remission criteria were included. The final remission decision was made based on a comprehensive evaluation of clinical status, laboratory markers, ASDAS and BASDAI scores, and findings from a detailed physical examination. In particular, any positive enthesitis findings during systematic physical examination – such as localized tenderness at predefined entheseal sites assessed by moderate digital pressure – were considered an exclusion criterion for remission, irrespective of laboratory or composite disease activity scores. Participants were subsequently divided into 2 groups according to their treatment regimen: those receiving biologic agents and those maintained on NSAIDs.

Clinical assessment

Demographic and clinical data, including age, gender, body mass index (BMI), disease duration, family history of SpA, smoking status, and current medications, were collected through standardized interviews and medical record reviews. The type and duration of biologic therapies were documented. A comprehensive physical examination was conducted by the same experienced rheumatologist (E.D.E.) to ensure consistency across evaluations. Pressure-induced tenderness was systematically assessed at entheseal sites corresponding to those evaluated by US.

Ultrasonographic assessment

Ultrasound evaluations were performed on the same day as clinical examinations by a different experienced

rheumatologist (S.B.) who was blinded to the patients' clinical data. A Logiq-E ultrasound system (General Electric, Wauwatosa, WI, USA) equipped with a 7–13 MHz linear transducer was used for the evaluations. The following bilateral entheseal sites were scanned: quadriceps tendon insertion, proximal and distal patellar tendon insertions, Achilles tendon insertion, and plantar fascia insertion.

For US positioning, the elbow enthesis was examined with the elbow flexed at 30–45°, the knee was assessed in the supine position with 30° flexion, and the heel was evaluated with the patient prone and the feet hanging neutrally over the edge of the examination table. All abnormalities were verified using 2 perpendicular planes to minimize anisotropy artifacts. The definition and scoring of enthesitis were based on the Outcome Measures in Rheumatology (OMERACT) US criteria. According to OMERACT, enthesitis is characterized by elementary lesions at the entheseal site, including hypoechogenicity, increased thickness, PD signal, bone erosion, enthesophyte formation, and calcifications [7]. Enthesitis severity was quantified by 2 composite scores: the inflammation score (sum of hypoechogenicity, thickening, and PD signal) and the structural damage score (sum of enthesophyte, calcification, and bone erosion). Each elementary lesion was graded semi-quantitatively from 0 to 3 based on severity (0: absent, 1: mild, 2: moderate, 3: severe). The total US enthesitis score was calculated as the sum of the inflammation and structural damage scores for each entheseal site. This method enabled a standardized and comprehensive evaluation of active inflammation and chronic structural changes at the entheseal insertions [8]. Power Doppler settings were standardized using a pulse repetition frequency of 500 Hz, a low wall filter, and maximal color gain without background noise below the bony cortex. Both longitudinal and transverse images were acquired for each entheseal site.

Statistical analysis

Continuous variables were expressed as means ±standard deviations (SD), and categorical variables were presented as frequencies and percentages. Differences in ultrasonographic scores between groups were analyzed using the Kruskal-Wallis test, followed by the Mann-Whitney *U* test for post hoc comparisons. Categorical variables were compared using the χ^2 test. Correlations between clinical variables and US scores were assessed using Spearman's rank correlation coefficient. A p-value of < 0.05 was considered statistically significant. Statistical analyses were conducted using SPSS version 29.0 (IBM Corp., Armonk, NY, USA).

Bioethical standards

The study was approved by the Ethics Committee of Adana City Training and Research Hospital, Turkey (decision number: 1627, 18.11.2021), and all participants provided written informed consent.

Results

The study aimed to examine the distribution of US findings among 72 patients with r-axSpA, categorized based on their medication usage into NSAID users (n = 23) and biologic agent users (n = 49). Ultrasound findings were analyzed at predefined entheseal sites using standardized scoring (Table I). In our cohort, the quadriceps tendon was the most frequently affected site, with US abnormalities observed in 98.6% of patients. This was followed by the distal patellar tendon (94.4%) and the Achilles tendon and plantar fascia, each involving 70.8% of patients. The proximal patellar tendon also showed a notable involvement rate, with abnormalities detected in 61.1% of patients. Regarding specific pathologies, hypoechogenicity was found in 22.2% of quadriceps tendons, 8.3% of proximal patellar tendons, 16.7% of distal patellar tendons, 25.0% of Achilles tendons, and 5.6% of plantar fasciae. Tendon thickening was most commonly observed at the distal patellar tendon (94.4%) and quadriceps tendon (63.9%). Enthesophyte formation was frequent in the quadriceps (63.9%), distal patellar (94.4%), and Achilles tendons (50.0%), whereas bone erosion was notably prevalent at the quadriceps (86.1%) and distal patellar tendons (66.7%). In contrast, calcifications and abnormal PD signals were rare across all evaluated sites (< 2%).

When stratified by treatment groups, NSAID users showed higher frequencies of quadriceps thickening (78.3% vs. 57.1%) and enthesophyte formation (78.3% vs. 57.1%) compared to biological agent users. Bone erosion at the quadriceps tendon was also slightly higher in NSAID users (95.7%) compared to biologic users (81.6%) (Table I). Despite these differences, the overall pattern of entheseal abnormalities was consistent across both groups, indicating a high burden of structural pathology independent of treatment modality.

Biochemical parameters further revealed that NSAID users exhibited significantly higher systemic inflammatory markers compared to biologic users. Mean CRP levels were 0.62 ±0.53 mg/dl in NSAID users vs. 0.41 ±0.27 mg/dl in biologic users (p = 0.027), while mean ESR values were 11.91 ±7.72 mm/h vs. 7.65 ±5.66 mm/h, respectively (p = 0.010). Although Axial Spondyloarthritis Disease Activity Score with CRP score (ASDAS-CRP) were numerically higher among NSAID users (2.06 ±0.43)

Table I. Ultrasonographic findings of patients

	Group	Hypoechogenicity [*n* = positive/ total (%)]	Thickening [*n* = positive/ total (%)]	PD signal [*n* = positive/ total (%)]	Calcification [*n* = positive/ total (%)]	Enthesophyte [*n* = positive/ total (%)]	Bone erosion [*n* = positive/ total (%)]	Sum [*n* = positive/ total (%)]
QU	NSAID (*n* = 23)	5/23 (21.7)	18/23 (78.3)	0/23 (0.0)	0/23 (0.0)	18/23 (78.3)	22/23 (95.7)	22/23 (95.7)
	Biologics (*n* = 49)	11/49 (22.4)	28/49 (57.1)	1/49 (2.0)	1/49 (2.0)	28/49 (57.1)	40/49 (81.6)	49/49 (100.0)
	All patients (*N* = 72)	16/72 (22.2)	46/72 (63.9)	1/72 (1.4)	1/72 (1.4)	46/72 (63.9)	62/72 (86.1)	71/72 (98.6)
PP	NSAID (*n* = 23)	2/23 (8.7)	18/23 (78.3)	0/23 (0.0)	0/23 (0.0)	18/23 (78.3)	18/23 (78.3)	18/23 (78.3)
	Biologics (*n* = 49)	4/49 (8.2)	26/49 (53.1)	0/49 (0.0)	0/49 (0.0)	26/49 (53.1)	26/49 (53.1)	26/49 (53.1)
	All patients (*N* = 72)	6/72 (8.3)	44/72 (61.1)	0/72 (0.0)	0/72 (0.0)	44/72 (61.1)	44/72 (61.1)	44/72 (61.1)
DP	NSAID (*n* = 23)	5/23 (21.7)	22/23 (95.7)	0/23 (0.0)	2/23 (8.7)	22/23 (95.7)	17/23 (73.9)	22/23 (95.7)
	Biologics (*n* = 49)	7/49 (14.3)	46/49 (93.9)	0/49 (0.0)	5/49 (10.2)	46/49 (93.9)	31/49 (63.3)	46/49 (93.9)
	All patients (*N* = 72)	12/72 (16.7)	68/72 (94.4)	0/72 (0.0)	7/72 (0.0)	68/72 (94.4)	48/72 (66.7)	68/72 (94.4)
Achilles	NSAID (*n* = 23)	6/23 (26.1)	12/23 (52.2)	0/23 (0.0)	0/23 (0.0)	12/23 (52.2)	11/23 (47.8)	12/23 (52.2)
	Biologics (*n* = 49)	12/49 (24.5)	24/49 (49.0)	0/49 (0.0)	0/49 (0.0)	24/49 (49.0)	22/49 (44.9)	39/49 (79.6)
	All patients (*N* = 72)	18/72 (25.0)	36/72 (50.0)	0/72 (0.0)	0/72 (0.0)	36/72 (50.0)	33/72 (45.8)	51/72 (70.8)
PF	NSAID (*n* = 23)	1/23 (4.3)	11/23 (47.8)	0/23 (0.0)	0/23 (0.0)	11/23 (47.8)	10/23 (43.5)	11/23 (47.8)
	Biologics (*n* = 49)	3/49 (6.1)	23/49 (46.9)	0/49 (0.0)	0/49 (0.0)	23/49 (46.9)	18/49 (36.7)	40/49 (81.7)
	All patients (*N* = 72)	4/72 (5.6)	34/72 (47.2)	0/72 (0.0)	0/72 (0.0)	34/72 (47.2)	28/72 (38.9)	51/72 (70.8)

AC – Achilles tendon, DP – distal patellar tendon, PF – plantar fascia, PP – proximal patellar tendon, QU – quadriceps.

compared to biologic users (1.85 ±0.54), the difference was not statistically significant (p = 0.113) (Table II). No significant differences were observed between the 2 groups regarding age, BMI, disease duration, smoking status, BASDAI, or Bath Ankylosing Spondylitis Functional Index (BASFI) scores (Table II).

Ultrasonography-based enthesitis scoring was performed for all patients, incorporating both inflammatory and structural components. The mean inflammation score, reflecting the cumulative burden of hypoechogenicity, thickening, and PD signal positivity, was 4.85 ±4.37 across the cohort, with NSAID users showing a mean

Table II. Demographic characteristics and clinical parameters of patients

Parameter	NSAID users (n = 23)	Biologic agent users (n = 49)	All patients (N = 72)	p
Age [years] (mean ±SD)	43.83 ±9.91	39.24 ±9.74	40.71 ±9.96	0.071
Sex [n (%)]				
Male	10 (43.5)	36 (73.5)	46 (63.9)	0.013*
Female	13 (56.5)	13 (26.5)	26 (36.1)	
BMI [kg/m^2] (mean ±SD)	27.39 ±5.26	27.01 ±4.32	27.13 ±4.61	0.748
BMI categories [n (%)]				
Underweight (< 18.5)	1 (4.3)	1 (2.0)	2 (2.8)	0.558
Normal (18.5–24.9)	6 (26.1)	18 (36.7)	24 (33.3)	
Overweight (25.0–29.9)	11 (47.8)	16 (32.7)	27 (37.5)	
Obese (≥ 30)	5 (21.7)	14 (28.6)	19 (26.4)	
Disease duration [years] (mean ±SD)	6.22 ±6.45	8.24 ±7.23	7.60 ±7.01	0.085
Duration of disease [n (%)]				
0–9.9 years	18 (78.3)	31 (63.3)	49 (68.1)	0.100
10–19.9 years	2 (8.7)	15 (30.6)	17 (23.6)	
≥ 20 years	3 (13.0)	3 (6.1)	6 (8.3)	
Smoking status [n (%)]				
Never smoked	15 (65.2)	24 (49.0)	39 (54.2)	0.100
Current smoker	7 (30.4)	21 (42.9)	28 (38.9)	
Former smoker	1 (4.3)	4 (8.2)	5 (6.9)	
Comorbid disease [n (%)]				
Present	2 (8.7)	4 (8.2)	6 (8.3)	0.939
Absent	21 (91.3)	45 (91.8)	66 (91.7)	
Family history [n (%)]				
Present	16 (69.6)	20 (40.8)	36 (50.0)	0.063
Absent	7 (30.4)	27 (55.1)	34 (47.2)	
Unknown	0 (0)	2 (4.1)	2 (2.8)	
Inflammation score (mean ±SD)	3.96 ±3.64	5.27 ±4.65	4.85 ±4.37	0.239
Tissue damage score (mean ±SD)	5.39 ±4.06	6.94 ±4.57	6.44 ±4.44	0.170
Total US score (mean ±SD)	9.26 ±6.92	12.16 ±8.66	11.24 ±8.21	0.082
BASFI (mean ±SD)	2.62 ±1.69	2.43 ±1.47	2.50 ±1.50	0.310
BASDAI (mean ±SD)	3.03 ±1.25	3.06 ±1.70	3.10 ±1.60	0.478
CRP [mg/dl] (mean ±SD)	0.62 ±0.53	0.41 ±0.27	0.48 ±0.38	0.027*
ESR [mm/h] (mean ±SD)	11.91 ±7.72	7.65 ±5.66	9.01 ±6.64	0.010*
ASDAS-CRP [mg/dl] (mean ±SD)	2.06 ±0.43	1.85 ±0.54	1.92 ±0.52	0.113

**Significant p-values are shown in bold.*

ASDAS-CRP – Axial Spondyloarthritis Disease Activity Score with C-reactive protein, BASDAI – Bath Ankylosing Spondylitis Disease Activity Index, BASFI – Bath Ankylosing Spondylitis Functional Index, BMI – body mass index, CRP – C-reactive protein, ESR – erythrocyte sedimentation rate, NSAIDs – nonsteroidal anti-inflammatory drugs, US – ultrasound.

Table III. Demographic characteristics and clinical parameters of patients with total US enthesopathy score ≥ 20 (*n* = 7)

Parameter	Patients with US enthesitis score ≥ 20 (*n* = 7)
Age [years] (mean ±SD)	45.29 ±11.44
Sex [*n* (%)]	
Male	6 (85.7)
Female	1 (14.3)
BMI [kg/m^2] (mean ±SD)	32.42 ±4.75
BMI categories [*n* (%)]	
Underweight (< 18.5)	0 (0)
Normal (18.5–24.9)	0 (0)
Overweight (25.0–29.9)	2 (28.6)
Obese (≥ 30)	5 (71.4)
Disease duration [months] (mean ±SD)	7.86 ±4.53
Duration of disease [*n* (%)]	
0–9.9 years	5 (71.4)
10–19.9 years	2 (28.6)
≥ 20 years	0 (0)
Smoking status [*n* (%)]	
Never smoked	2 (28.6)
Current smoker	2 (28.6)
Former smoker	3 (42.9)
Comorbid disease [*n* (%)]	
Present	1 (14.3)
Absent	6 (85.7)
Family history [*n* (%)]	
Present	3 (42.9)
Absent	4 (57.1)
Unknown	0 (0)
Inflammation score (mean ±SD)	14.71 ±4.19
Tissue damage score (mean ±SD)	15.71 ±2.98
Total US score (mean ±SD)	30.43 ±5.83
BASFI (mean ±SD)	2.20 ±1.07
BASDAI (mean ±SD)	2.21 ±1.48
CRP [mg/dl] (mean ±SD)	0.62 ±0.46
ESR [mm/h] (mean ±SD)	11.43 ±7.50
ASDAS-CRP [mg/dl] (mean ±SD)	1.81 ±0.68

ASDAS-CRP – Axial Spondyloarthritis Disease Activity Score with C-reactive protein, BASDAI – Bath Ankylosing Spondylitis Disease Activity Index, BASFI – Bath Ankylosing Spondylitis Functional Index, BMI – body mass index, CRP – C-reactive protein, ESR – erythrocyte sedimentation rate, US – ultrasound.

of 3.96 ±3.64 and biologic users 5.27 ±4.65 (p = 0.239). The mean tissue damage score, calculated from calcification, enthesophyte formation, and bone erosion, was 6.44 ±4.44, with subgroup means of 5.39 ± 4.06 for NSAID users and 6.94 ±4.57 for biologic users (p = 0.170). The mean total US enthesitis score, representing the sum of inflammation and tissue damage scores, was 11.24 ± 8.21 overall, 9.26 ±6.92 for NSAID users, and 12.16 ±8.66 for biologic users (p = 0.082; Table II).

A subgroup analysis identified 7 patients (9.7%) with total US enthesitis scores exceeding 20 points. In this subgroup, the mean inflammation score was 14.71 ±4.19, the mean tissue damage score was 15.71 ±2.98, and the mean total enthesitis score reached 30.43 ±5.83. All 7 patients were overweight or obese (mean BMI 32.42 ±4.75) and were receiving biologic therapy. Six out of 7 were male (85.7%). Despite biologic treatment, these patients demonstrated persistent and substantial entheseal inflammation and structural damage, suggesting a possible association between high entheseal burden, obesity, and treatment-resistant enthesitis (Table III).

Overall, this study's findings highlight a high prevalence of US entheseal abnormalities in r-axSpA patients, independent of current treatment strategies, and underscore the need for comprehensive entheseal assessment in routine clinical practice.

Discussion

Enthesitis is a hallmark of r-axSpA, the prototype of SpA. There is evidence that enthesitis may still be active in r-axSpA patients even when using biological agent therapy or NSAIDs. We could not find any study showing the superiority of biological agents and NSAIDs that have been proven effective in treating enthesitis. In this respect, our study fills the gap in the literature.

Several recent studies have highlighted the limitations of clinical evaluation in accurately detecting enthesitis. Masmitja et al. [9] demonstrated that conventional physical examination alone has insufficient sensitivity, complicating the identification of true remission in patients with r-axSpA. Similarly, grey-scale US has revealed subclinical Achilles enthesitis in asymptomatic patients, emphasizing the need for imaging modalities in disease monitoring [10, 11]. Our study supports these findings, showing that most patients – despite meeting remission criteria according to BASDAI and ASDAS – had entheseal abnormalities on US. In particular, at least 1 pathological US finding was observed in the quadriceps tendon in 98.6% of patients and the Achilles tendon in over 70%. This suggests that imaging-detected enthesitis may persist even when patients are clinically silent. Furthermore, Schett et al. [12] underscored the pathogenic relevance of the interleu-

kin (IL)-17 and IL-23 axis in enthesitis and emphasized that current biological treatments – although effective – do not fully address subclinical inflammation. Patients receiving biologic agents in our cohort still exhibited high total enthesitis scores, reinforcing the need to re-evaluate treatment response using imaging criteria. Wu et al. [13] also strongly recommended routine US in enthesitis assessment; our findings confirm the utility of this approach, especially in remission states where physical examination and acute-phase reactants are not fully reliable.

The quadriceps tendon and distal patellar tendon are of particular importance. In a study conducted on patients diagnosed with PsA and psoriasis, statistically higher rates of enthesitis were detected in both enthesitis regions in patients diagnosed with PsA [14]. This is an interesting finding, and in our study, US findings were most frequently detected in the quadriceps tendon and distal patellar tendon in all patients (Table I). Structural damage was more commonly detected in our study. These results indicate the necessity of evaluating these 2 regions in SpA group diseases.

In our study, no statistically significant differences were observed between NSAID and biologic agent groups regarding disease duration, comorbidities, smoking status, family history, BMI, BASDAI, BASFI, and ASDAS-CRP scores. Although both groups fulfilled clinical remission or low disease activity criteria, persistent entheseal abnormalities were frequently detected by US. This discrepancy suggests that conventional clinical and biochemical measures may not fully capture the underlying entheseal pathology in patients with r-axSpA. Although NSAIDs and biologic agents modulate inflammation through different mechanisms [15, 16], our findings did not reveal a clear difference in US enthesitis scores between the 2 treatment groups. This may suggest that factors beyond pharmacologic effects, such as mechanical stress, baseline disease severity, or interindividual variability, could contribute to persistent entheseal changes. Interestingly, despite similar US scores, systemic inflammatory markers (ESR and CRP) were statistically significantly higher in the NSAID group. This observation could indicate more effective systemic inflammation control by biologic therapies; however, the cross-sectional nature of our study precludes causal interpretation. Notably, the frequent detection of US abnormalities in patients deemed to be in remission according to BASDAI and ASDAS-CRP underscores the limitations of relying solely on clinical and laboratory indices. These results align with recommendations advocating for the integration of musculoskeletal US into disease activity assessment frameworks for r-axSpA [13]. Overall, our findings suggest that US evaluation provides valuable complementary information in assessing disease status, potentially identifying patients with ongoing subclinical entheseal inflammation who may otherwise be overlooked by traditional remission criteria. Further longitudinal studies are warranted to elucidate the clinical relevance of persistent entheseal abnormalities and their implications for long-term outcomes in r-axSpA.

The main target in treating AS should be a composite measure that includes clinical findings, measures of inflammation, physical function, quality of life, and radiographic progression. It should be comprehensive enough to cover the main areas of the disease and be helpful in clinical trials and clinical practice. Currently used measures of disease activity such as the BASDAI and ASDAS and laboratory findings such as ESR and CRP do not objectively consider extra-articular findings. The BASDAI includes 6 items measuring fatigue, back, neck, or hip pain, peripheral joint pain and swelling, localized tenderness (including enthesitis), and morning stiffness duration and severity. However, the BASDAI is purely subjective, and no objective measure of inflammation exists. The BASDAI does not consider the extra-articular features of axSpA [17]. Axial Spondyloarthritis Disease Activity Score is much more sensitive to disease change and is ideal for targeting [18, 19]. In this scoring, CRP values were also added to evaluate the presence of inflammation. However, CRP is elevated in only 40–60% of patients with r-axSpA; therefore, patients with axSpA with normal baseline CRP may be considered in remission, but this may not be the case. In clinical trials, only a few patients achieve the established ASDAS targets (ASDAS < 2.1). In the ABILITY 1 study, 15% of 176 patients reached the target, whereas 27% of patients in the GORAISE study did [20, 21]. The concept of minimal disease activity (MDA) in PsA takes into account not only peripheral arthritis but also the involvement of the skin, entheses, and fingers (dactylitis) [22]. There is no such definition of MDA in AS yet. Therefore, more objective evaluations, such as those of the US, should be included in these definitions. Despite achieving low BASDAI and ASDAS-CRP scores in our study, many patients exhibited apparent entheseal abnormalities in the US – highlighting a potential discordance between clinical remission and entheseal inflammation. Power Doppler positivity was rare, yet total enthesitis scores were markedly elevated in some patients, indicating that reliance on the PD signal alone may underestimate disease burden. The lack of a validated cut-off value in OMERACT scoring systems for defining "high enthesitis burden" limits our ability to classify patients based on disease severity using US alone. This allowed us to adopt a data-driven approach in which patients with total scores > 20 were analyzed as a high-score subgroup. Although

not standardized, it provides a preliminary framework for identifying patients with disproportionate entheseal involvement despite apparent clinical stability. The absence of a MDA definition in r-axSpA, unlike in PsA, further underscores the need for composite indices that incorporate imaging modalities such as US. Our findings suggest that incorporating structured US assessment – guided by validated frameworks such as OMERACT – may enhance the sensitivity of remission evaluation and support more individualized treatment strategies.

Interestingly, although there was no statistically significant difference in total US-based enthesitis scores between the NSAID and biologic agent groups, the patients with the highest scores were exclusively in the biologic treatment group. This pattern may reflect a treatment selection effect, as biologics are generally prescribed for patients with more severe or refractory diseases unresponsive to NSAIDs. Patients receiving biologic agents likely had a higher baseline disease burden in this context. Additionally, it is important to recognize that some components of the US-based enthesitis score, particularly structural changes such as bone erosion, enthesophyte formation, or calcification, reflect chronic and potentially irreversible tissue damage. These lesions may persist despite adequate control of inflammation and are unlikely to regress even with effective biologic therapy, especially if the treatment was initiated late in the disease course.

Therefore, the persistence of high enthesitis scores in the biological group may not necessarily indicate treatment failure but may instead reflect structural damage accumulated prior to therapy. This observation highlights the need to interpret US findings not only in the context of disease activity but also taking into consideration the timing and goals of therapy, particularly distinguishing between active inflammation and chronic structural sequelae.

Study limitations

While the limited sample size and lack of homogeneity across treatment groups represent important limitations of our study, these factors also reflect the heterogeneity encountered in real-world r-axSpA populations. Patients with higher total enthesitis scores (> 20) tended to have BMI values above 25, raising the possibility that mechanical factors may influence US findings independently of inflammatory activity. However, this relationship should be interpreted cautiously and warrants further investigation in larger, prospective cohorts. An important strength of our study lies in its demonstration that reliance solely on the power of the Doppler signal may underestimate the true extent of entheseal pathology. Nevertheless, several patients without PD signals exhibited high total enthesitis scores, highlighting the utility of composite scoring systems and suggesting that PD negativity does not necessarily indicate the absence of clinically meaningful disease activity. Additional limitations should also be considered. The cross-sectional design precluded the assessment of temporal relationships or treatment response over time. Moreover, we adopted a data-driven cut-off of > 20 to define high entheseal burden, yet no validated threshold currently exists in the literature, limiting comparability. A single examiner performed all ultrasonographic assessments using 1 US system, reducing interobserver variability and potentially limiting external generalizability. Machine sensitivity or operator-dependent factors may influence the low PD signal rates observed. Finally, the absence of a reference imaging modality such as magnetic resonance imaging prevents further validation of our ultrasonographic findings.

Conclusions

Musculoskeletal US may detect subclinical entheseal involvement in r-axSpA patients who fulfill standard remission or low disease activity criteria. Our findings support the integration of structured US assessment – guided by OMERACT scoring – into routine evaluation strategies to better capture residual disease activity and guide individualized treatment decisions.

Key points:

1. Integrating total entheseal scoring by US into evaluating patients with low disease activity based on ASDAS and BASDAI may enhance clinicians' ability to assess remission more comprehensively.
2. No significant difference was observed in US-based enthesitis scores in patients in clinical remission receiving either NSAIDs or biologic agents. This finding supports individualized treatment rather than relying solely on treatment class.
3. Ultrasound assessment may serve as a valuable adjunct in routine monitoring of patients with r-axSpA and could provide additional information to guide treatment decisions and modifications.

Disclosures

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Data availability: The data that support the findings of this study are available on request from the corresponding author (B.O.).

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