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Ultrasonographic evaluation of Achilles tendon: Is there any difference between ankylosing spondylitis, non-radiographic axial spondyloarthropathy and controls?

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Abstract

Purpose: The aim is to evaluate Achilles tendon enthesopathy with ultrasound (US) in ankylosing spondylitis (AS) and non-radiographic axial SpA (nr-axSpA) patients and controls, and compare these groups in terms of associations between disease activity parameters and ultrasonographic Achilles enthesitis signs.

Methods: A total of 24 AS and 20 nr-axSpA patients fulfilling the Assessment in Spondyloarthritis International Working Group criteria for axSpA and 30 controls were enrolled. Demographic characteristics, erythrocyte sedimentation rate, C-reactive protein (CRP), human leukocyte antigen (HLA)-B27, Bath AS Disease Activity Index, Bath AS Functional Index, Bath AS Metrology Index, Maastricht AS Enthesitis Score (MASES), AS Disease Activity Score-CRP, modified Stoke AS Spine Score (m-SASSS) scores and ultrasonographic findings were noted.

Results: HLA-B27 positivity, extra-articular and peripheral involvement, disease activity, functional status, mean m-SASSS, ultrasonographic gray scale (GS) and total scores were similar between AS and nr-axSpA groups. In GS, tendon echotexture scores were significantly different across all groups (0.812 ± 0.384 in AS, 0.575 ± 0.466 in nr-axSpA, 0.017 ± 0.091 in controls; $P < .001$). Entheseal calcification scores were similar in AS and nr-axSpA patients, and higher than controls ($P = .001$). Bone profile scores were similar in patients with AS and nr-axSpA, and higher than controls ($P = .010$). When the correlations between US findings and disease activity and functional status were considered, power Doppler US (PDUS) and MASES total scores were positively correlated in the AS group ($P = .045$; $r = .41$).

Conclusion: AS and nr-axSpA patients were found to be similar in various clinical, functional, and US findings indicating that these 2 entities are different phenotypic reflections of the same disease spectrum. The positive correlation between PDUS and MASES scores in AS patients substantiate the performance of MASES in evaluation of entheseal activity.

KEYWORDS

achilles, ankylosing spondylitis, enthesitis, non-radiographic axial spondyloarthritis, ultrasound

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1 | INTRODUCTION

Axial spondyloarthropathy (axSpA) comprises both early non-radiographic patients and ones with radiographic sacroiliitis defined by modified New York criteria. Along with emergence of the term non-radiographic axSpA (nr-axSpA), studies comparing ankylosing spondylitis (AS) and nr-axSpA regarding genetic, epidemiologic, and clinical features, treatment requirements, and response to therapy have accrued. Patients with nr-axSpA cause a considerable disease burden and have a probability to progress to the radiographic stage in time.[1]

Musculoskeletal ultrasound serves as a sensitive, noninvasive, rapid, and inexpensive tool for assessing the entheses. It can provide more objective and reliable indicators for evaluation of enthesis than physical examination.[2,3] Ultrasound is widely accessible with comparable sensitivity in showing superficial tissue inflammation to magnetic resonance imaging (MRI).[4] This case-control study aims to evaluate the Achilles tendon using ultrasonography (US) in AS and nr-axSpA patients and to compare these groups regarding associations between disease activity parameters and US Achilles enthesitis signs.

2 | METHODS

A total of 24 AS patients and 20 nr-axSpA patients applying to Ankara University Rheumatology Outpatient Clinic and 30 controls were enrolled. AS patients fulfilled the modified 1984 New York criteria[5] and nr-axSpA patients fulfilled the Assessment of Spondyloarthritis International Society (ASAS) criteria for axSpA.[6] Any inflammatory arthritis other than SpA, history of malignancy, active tuberculosis or other infection, hepatitis B and C infection, women in pregnancy or lactation, patients who had previous injections or surgical procedures to the Achilles tendon or retrocalcaneal bursa, or were receiving oral steroids, who had metabolic or chronic diseases such as hyperparathyroidism, Paget's disease or hypoparathyroidism, diabetes, fibromyalgia and so on, history of sports or physical activities that can cause Achilles enthesitis and disease duration of >24 months, were excluded.

The healthy controls were assigned from hospital stuff and patients' attendants. Clinico-demographic characteristics and laboratory results including presence of uveitis, dactylitis, inflammatory bowel disease (IBD), psoriasis, and enthesitis, erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) levels and human leukocyte antigen (HLA)-B27 were recorded. The Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), the Bath Ankylosing Spondylitis Metrologic Index (BASMI), the Bath Ankylosing Spondylitis Functional Index (BASFI), the Maastricht Ankylosing Spondylitis Enthesitis Score (MASES), and Ankylosing Spondylitis Disease Activity Score (ASDAS-CRP) were calculated. All patients were recently diagnosed and they were on non-steroidal anti-inflammatory drug treatment. Radiographic evaluation was performed using the modified Stoke Ankylosing Spondylitis Spinal Score (m-SASSS). The Outcome Measures in Rheumatology (OMERACT) scoring system was used for ultrasonographic grading of the Achilles tendon.[7] MRI evaluation were performed by radiologists while m-SASSS and US evaluation was carried out by 2 rheumatologists experienced in US. The study was approved by the Ethics Committee of Ankara University School of Medicine (Date: 06.03.2017 and number: 06-288-17) and informed consents were obtained from all patients.

2.1 | US scanning technique

The US examinations were performed in a darkened room by 2 rheumatologists (IS and GY), both for each patient, and were blinded to clinical data and patients' identities. Participants were questioned, examined, rested and their research forms were filled while being kept waiting for 15 minutes before US evaluation. The patients took a prone position, feet hanging off the examination table in a neutral position. Bilateral Achilles tendon US examinations were carried out using a multiplanar scanning technique with attention not to apply transducer pressure (GE Logio P5 Ultrasound, Serial number: GE-114118SU3. Device contents: ARTronic power supply and 1 linear probe).

Semi-quantitative US assessment was carried out according to a scoring system recently developed for rating Achilles enthesitis.[8] Scoring system was evaluated between 0-2:0, none; 1, mild–moderate; 2, severe.[9]

The 3 calculated scores for each patient and used parameters were:

(i) A power Doppler (PD) score indicating vascularity at 3 levels (tendon, bursa and enthesis), ranging from 0 to 12 with semi-quantitative scores (per patient)
(ii) A GS score: the echogenicity of enthesis and tendon (circumscribed hypoechoic areas with loss of fibrillar echotexture, calcifications appearing as intratendineous hyperechoic spots), the tendon thickness, presence of retrocalcaneal bursitis indicated by effusion, bone profile (bony cortex irregularities not including definite enthesophytes nor bone erosions) ranging from 0 to 32 with semi-quantitative scores (per patient)
(iii) A total score: the sum of PD and GS scores, ranging from 0 to 44 with semi-quantitative scores (per patient)[8] (Table 2).

2.2 | Statistical analysis

SPSS (version 11.5, Statistical Program for Social Sciences) pocket program was used for statistical analyses. Description of quantitative variables was expressed as mean, standard deviation (SD) and median, minimum-maximum. Description of qualitative variables was expressed as number (n) and percentage (%). Distribution of data was assessed with histograms and Kolmogorov-Smirnov test. For the comparison of the categorical data, Chi-square and Fisher's

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exact test were used. For comparison of mean or median values of continuous values Mann-Whitney *U* and analysis of variance tests were used. Kruskal-Wallis test was used for comparison of non-parametric data. Spearman's correlation coefficient was applied for determination of the correlation between clinical and ultrasonographic parameters.

3 | RESULTS

The mean age of the whole group was 34.05 ± 8.11 years and the mean body mass index (BMI) was 25.94 ± 5.06. The AS patients were 17 women (70.8%) and 7 men (29.2%), the nr-axSpA group was comprised of 13 women (65%) and 7 men (35%) while controls consisted of 20 women (66.7%) and 10 men (33.3%) (P = .910). The mean age of the control group was lower than AS patients (P = .025) and similar to nr-axSpA patients (P = .764). The median symptom duration was higher in AS patients: 36.5 (interquartile range [IQR] 54) months in nr-axSpA and 84 (99) months in AS patients (P = .009). The median diagnosis duration was similar between these groups: 12 (IQR 17) months in nr-axSpA and 3 (16) months in AS patients (P = .595). Medications did not differ significantly between AS and nr-axSpA groups (P = .876). When the groups were compared in terms of BMI, statistically significant difference was present (P = .023). AS patients and controls differed significantly (P = .036) while patients with AS and nr-axSpA did not differ in terms of BMI (P = .984). Furthermore, the median BMI, CRP, ESR, BASFI, BASDAI, BASMI, MASES, ASDAS-CRP, and total m-SASSS scores were similar between AS and nr-axSpA patients (P = .984, P = .540, P = .113, P = .953, P = .723, P = .333, P = .385, P = .487, P = .804, respectively) (Table 1). Also, HLA-B27 positivity rate, extra-articular and peripheral involvement, disease activity and functional status, mean m-SASSS, and GS and the total score (TS) were similar between AS and nr-axSpA groups (Table 2). In GS, tendon echotexture scores were significantly different across all groups (0.812 ± 0.384 in AS, 0.575 ± 0.466 in nr-axSpA, 0.017 ± 0.091 in controls; P < .001). Entheseal calcification scores were similar in AS and nr-axSpA patients, and higher than controls (P = .001). Bone profile scores were similar in AS and nr-axSpA patients, and higher than controls (P = .010) (Tables 2, 3). When the correlation between US findings and disease activity and functional status were considered, PD US and MASES TSs were positively correlated in the AS group (P = .045; r_s = .413) while other indices did not correlate significantly with the PD score (Table 4). The US findings are shown in Figures 1-5.

4 | DISCUSSION

In this study, extra-articular involvement rates except for IBD (P = .053), HLA-B27 status and fulfillment of the ASAS criteria were not different in radiographic and non-radiographic groups. Similar to our results, in a study to compare the clinical manifestations of AS and nr-axSpA, the patients in the 2 groups did not differ in the presence of arthritis and enthesitis, disease activity (BASDAI, ASDAS-CRP) and functional status (BASFI) and unlike our results, uveitis in AS patients were reported to be more prevalent in a meta-analysis.[10,11] In another retrospective study, patients with AS were more often men and had longer symptom duration. Median levels of acute-phase reactants (CRP, ESR) were significantly higher in patients with AS.[12] In the present study, BASFI, BASDAI, BASMI, MASES, ASDAS-CRP, CRP, ESR were also similar between 2 groups. Similar to our results in a study on a total of 288 axSpA patients, 187 of whom had AS, BASMI values were higher in the AS group than nr-axSpA, while BASDAI, ASDAS, BASFI, ESR and CRP did not differ significantly between these 2 groups.[13] The discrepancies between both various studies and our results indicate that these groups are different phases of the same disease displaying similar disease burden.

In our study, there was no difference in m-SASSS scores between radiographic and non-radiographic patients. In a prospective longitudinal observational cohort study on patients with AS, both initial spinal radiographic damage and radiographic progression showed high variability among AS patients.[14] In another study on 100 consecutive patients with axSpA, signs of inflammation in MRI were significantly higher in AS patients while both groups did not differ regarding health status, disease activity, and physical function, despite all being higher in patients with AS.[15] In a retrospective study, patients with nr-axSpA who converted to AS displayed higher radiographic changes and syndesmophytes on X-ray.[16]

In a systematic literature review, it was found that higher BMI was closely related with new bone formation including syndesmophytes, enthesophytes and also a higher m-SASSS. Fewer studies investigated the effect of BMI on peripheral enthesis which reported a moderate positive correlation between Madrid Sonographic Enthesitis Index (MASEI) scores and BMI. Gender was found to be a significant factor to influence this association in one study which showed correlation between US enthesophyte scores and BMI in males but not in females.[17] In another multicenter, case-control study with 225 consecutive AS patients and 95 age- and BMI-matched controls to explore the relationship between spinal new bone formation and US-determined Achilles enthesophytes, cervical and lumbar spine radiographs were taken. AS patients had significantly higher US enthesophyte scores than controls. The difference was significant in males but not in females. The enthesophyte scores significantly correlated with m-SASSS scores and the relationship was stronger in males. According to multiple regression analysis; BMI, age, enthesophyte scores, and the duration of disease were reported to be significantly associated to syndesmophytes in men. When other variables were constant, the higher US enthesophyte scores, the higher odds ratio was to have syndesmophytes.[18] Therefore, the significant difference in BMI (lower) and age (younger) in the controls may have contributed to less enthesitis due to mechanical stress or degeneration in our study. If the groups were homogeneous in terms of BMI, age and gender more reliable results would have been yielded.

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TABLE 1 Clinicodemographic characteristics of 3 groups of AS, nr-axSpA, and control

Parameter	Ankylosing spondylitis	nr-axSpA		Control		*P*
	Mean ± SD or median (min-max)	Mean ± SD	Median (min-max)	Mean ± SD	Median (min-max)	
Age, y	37.5 ± 5.6	33.4 ± 8.2		31.8 ± 9.0		**.030**
BMI, kg/m^2	27.4 ± 5.3	27.1 ± 5.3		24.0 ± 4.2		**.023**
Gender, % female	70.8	65		66.7		.910
Education, % high school and above	70.3	75		93.3		**.001**
Drugs						
NSAIDs	79.2	70		–		.876
NSAIDs + SSZ	8.3	10		–		
Symptom duration, mo	84 (12-300)	36.5 (2-204)		–		**.009**
Diagnosis duration, mo	3 (1-72)	12 (1-24)		–		.595
Inflammatory back pain, %	79.2	90.0		–		.428
Peripheral arthritis, %	20.8	45.0		–		.087
Enthesitis, %	62.5	60		–		.865
Uveitis, %	4.2	0.0		–		1.000
Dactylitis, %	8.3	15		–		.646
IBD, %	20.8	0.0		–		**.053**
HLA-B27 positivity, %	25	25		–		1.000
BASDAI	4.1 (0.6-7.0)	4.4 (1.2-7.4)		–		.723
BASFI	1.75 (0-7.2)	1.65 (0-4.8)		–		.953
BASMI	2 (0-5)	3 (0-4)		–		.333
MASES	4 (0-13)	3 (0-13)		–		.385
m-SASSS	12 (4-23)	13.5 (4-22)		–		.804
ASDAS-CRP	2.5 ± 0.7	2.4 ± 0.8		–		.487
CRP	2.7 (0.1-38.3)	2.9 (1-14.1)		–		.540
ESR	11 (3-34)	36.5 (1-18)		–		.113

Note: Bold values are statistically significant $P < .05$.

Abbreviations: ASDAS-CRP, Ankylosing Spondylitis Disease Activity Score; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Spondylitis Functional Index; BASMI, Bath Ankylosing Spondylitis Metrologic Index; BMI, body mass index; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; MASES, Maastricht Ankylosing Spondylitis Enthesitis Score; m-SASSS, modified Stoke Ankylosing Spondylitis Spinal Score; nr-axSpA, non-radiographic axial spondyloarthropathy.

In 2 follow-up studies, as the studies were short-term and US findings indicating damage like bone profile changes and calcifications were not expected to change within this period, only US findings reflecting inflammation were included in the final scores.[3,8] Due to our cross-sectional and case-control design, entheseal calcification and bone profile scores were higher than controls despite being similar in AS and nr-axSpA patients.

In a study to compare clinical examination findings with PD US to detect the abnormalities of entheseal regions on 36 patients with AS, the most commonly observed US abnormalities were enthesophytes, hypoechogenicity, calcifications, and tendon thickening. They found erosions and PD US signals in 9.7% and 6% of the entheseal regions respectively and the findings favoring entheseal abnormalities by clinical examination had a poor likelihood ratio for detected US abnormalities. According to these researchers, PD US allows detection of structural and inflammatory abnormalities of the enthesis in AS and may complement the role of physical examination for assessment of enthesitis.[19] In a prospective clinical trial on 30 patients with SpA and 30 controls aged <45 years, conventional radiography, GS US including PD US, and MRI of symptomatic areas (knees or heels) were performed for evaluation of inflammatory and structural changes. Given the finding that the erosive changes at the heel enthesis were more frequent in patients with SpA, it was concluded that differentiation between SpA and non-SpA was only possible relying on structural but not inflammatory changes in the heels and knees of symptomatic patients. These findings propound that SpA is associated with erosive changes at entheseal sites whereas inflammation is of minor importance.[20] Similarly, bone profile changes

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TABLE 2 Ultrasound findings of ankylosing spondylitis and non-radiographic axial spondyloarthropathy (nr-ax SPA) patients, and controls

	Ankylosing spondylitis		nr-axSpA		Control		
Parameters	Mean ± SD	Median (min-max)	Mean ± SD	Median (min-max)	Mean ± SD	Median (min-max)	*P*
TE 1	0.812 ± 0.384	1.0 (0-1.0)	0.575 ± 0.466	0.75 (0-1.0)	0.017 ± 0.091	0 (0-0.5)	**<.001**
TE 2	0.083 ± 0.190	0 (0-0.5)	0.750 ± 0.183	0 (0-0.5)	0.0 ± 0.0	0 (0-0)	.073
TE 3	0.104 ± 0.254	0.0 (0-1.0)	0.075 ± 0.244	0 (0-0.1)	0.117 ± 0.252	0 (0-1.0)	.684
TS	0.375 ± 0.629	0.0 (0-2.0)	0.250 ± 0.444	0 (0-1.5)	0.067 ± 0.172	0 (0-0.5)	.079
TV	0.063 ± 0.224	0.0 (0-1.0)	0.0 ± 0.0	0 (0-0)	0.0 ± 0.0	0 (0-0)	.121
EE 1	0.021 ± 0.102	0 (0-0.5)	0.025 ± 0.111	0 (0-0)	0.0 ± 0.0	0 (0-0)	.494
EE 2	0.563 ± 0.425	0.5 (0-1.0)	0.525 ± 0.472	0.5 (0-1.0)	0.167 ± 0.330	0 (0-1.0)	**.001**
EV	0.042 ± 0.204	0.0 (0-1.0)	0.0 ± 0.0	0 (0-0)	0.0 ± 0.0	0 (0-0)	.353
BS	0.667 ± 0.637	0.5 (0-2.0)	0.350 ± 0.366	0.5 (0-1.0)	0.467 ± 0.571	0.25 (0-2.0)	.267
BV	0.042 ± 0.141	0 (0-0.5)	0.0 ± 0.0	0 (0-0)	0.0 ± 0.0	0 (0-0)	.121
BP	0.333 ± 0.524	0.0 (0-2.0)	0.150 ± 0.328	0 (0-1.0)	0.050 ± 0.201	0 (0-1.0)	**.010**

Note: Calcaneal enthesophytes, new bone formation at enthesis–bone junction.[a] Calcaneal bone erosions, discontinuity of the bone profile seen in 2 perpendicular planes (score 0, no bone erosions; score 1, between 0.1 and 2 mm; score 2, higher than 2 mm). [a]Scoring system ranging from 0 to 2:0, none; 1, mild–moderate; 2, severe.

Abbreviations: BP, Bone profile (Calcaneal bony cortex irregularities not including definite enthesophytes nor bone erosions[a] Calcaneal enthesophytes; new bone formation at enthesis-bone junction [a]Calcaneal bone erosions; discontinuity of the bone profile see in two perpendicular planes (score 0: no bone erosions; score 1: between 0.1 and 2 mm; score 2: higher than 2 mm); BS, Bursal size (Bursal enlargement is defined as an increase in diameter of the bursa. With well defined, compressible , anechoic or hypoechoic area inside (score 0: less than 2 mm; score 1: between 2-4 mm; score 2: higher than 4 mm); BV, Bursal vascularity (Power Dopplr signal within the bursa[a]); EE, Entheseal echogenicity (1: Circumscribed hypoechoic areas with loss of fibrillar echotexture[a]. 2: Calcifications appearing as intratendineous hyperechoic spots[a]); EV, Entheseal vascularity (Power Doppler signal of the enthesis[a]); TE, Tendon echogenicity (1: Loss of the typical ''fibrillar'' echotexture. 2: Focal hypoechoic areas with loss of fibrillar echotexture[a]. 3: Calcifications appearing as intratendineous hyperechoic spots); TS, Tendon size (Tendon thickness was measured at the insertion of the deeper margin into the calcaneal bone (score 0: .5.3 mm; score 1: between 5.3 and 6.3; score 2: higher than 6.3 mm); TV, Tendon vascularity (Intratendineous power Doppler signal.[a]).

Bold values are statistically significant $P < .05$.

TABLE 3 Ultrasound findings of AS and nr-axSPA patients, and controls

		n	Mean	SD	Median	Min.	Max.	*P*
GS score	AS	24	5.92	3.46	4.50	2.00	14.00	**<.001**
	nr-axSPA	20	4.05	2.80	3.50	0.00	9.00	
	Control	30	1.73	1.89	1.00	0.00	7.00	
PD score	AS	24	0.29	1.08	0.00	0.00	5.00	.12
	nr-axSPA	20	0.00	0.00	0.00	0.00	0.00	
	Control	30	0.00	0.00	0.00	0.00	0.00	
Total score	AS	24	6.21	4.25	4.50	2.00	19.00	**<.001**
	nr-axSPA	20	4.05	2.80	3.50	0.00	9.00	
	Control	30	1.73	1.89	1.00	0.00	7.00	

Note: Bold values are statistically significant $P < .05$.

Abbreviations: AS, ankylosing spondylitis; GS, gray-scale; nr-axSpA, non-radiographic axial spondyloarthropathy; PD, power Doppler.

including erosions were similar in AS and nr-axSpA patients, and higher than controls in our study.

In another study from our country, BASDAI and total physical examination scores of enthesitis and MASEI scores were positively correlated in SpA patients.[21] Also, we found significant moderate correlation between MASES scores and PD scores but not GS scores in patients with AS in the present study. In a prospective study with 60 AS patient to investigate the correlations between clinical, radiographic, and sonographic scores of enthesitis, the radiographic score correlated with the visual analog scale (VAS), BASDAI, and BASFI. The sonographic score for acute enthesitis correlated only with the MASES, and the sonographic score for chronic enthesitis correlated with none of the clinical scores. The PD US score correlated with the VAS pain score, BASDAI, BASFI, and AS Quality of Life Questionnaire (ASQoL). The overall sonographic score correlated with the MASES and Spondyloarthritis

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TABLE 4 Correlation of PD scores and disease activity and functional status in the AS group

Parameters	r_s	*P*
BASDAI Q4	.028	.896
BASDAI Total	.087	.687
CRP	.369	.076
ESR	.213	.318
BASMI	.218	.305
MASES	**.413**	**.045**
ASDAS-CRP	.255	.229
m-SASSS	.020	.926

Note: Bold values are statistically significant $P < .05$.

Abbreviations: ASDAS-CRP, Ankylosing Spondylitis Disease Activity Score; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASMI, Bath Ankylosing Spondylitis Metrologic Index; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; MASES, Maastricht Ankylosing Spondylitis Enthesitis Score; m-SASSS, modified Stoke Ankylosing Spondylitis Spinal Score; PD, power Doppler; Q4, 4th question.

Research Consortium of Canada Enthesitis Index (SPARCC).[22] In a study on 708 patients of the DESIR (Devenir des Spondyloarthrites Indifférenciées Récentes) cohort to investigate the association between US enthesis abnormalities and disease activity, they reported no association between US scores with BASDAI, CRP and inflammatory lesions on sacroiliac joint and spine MRI. However, unlike our results, there was a correlation between US structural and PD US scores and the m-SASSS.[23] The overwhelming difference in number of patients enrolled in these studies may explain the difference in results.

Question 4 of BASDAI is related to enthesitis. It was reported in previous studies that question 4 had higher correlation with the clinical enthesitis scores such as MASES, Leeds Enthesitis Index, and the SPARCC than the remaining items of the BASDAI.[24] Therefore, we investigated whether there was an association between the 4th question of the BASDAI and US findings. However, we did not find significant correlation with US findings.

In a study on 40 patients with axSpA and 27 patients with RA and 30 healthy subjects to analyze the ultrasonographic features of the Achilles tendon, paratenon, and enthesis, the relationships between these findings and clinical and functional parameters, Achilles tendon thickness, paratenon thickness, and echogenicity were examined bilaterally. Similar to our study, the fibrillar pattern of the Achilles tendon was damaged in patients with axSpA compared to RA patients and healthy subjects. Also, the Achilles tendon and paratenon were thicker in axSpA patients than RA patients and healthy subjects. Unlike in our study, there were positive correlations between BASDAI and BASFI scores and the Achilles enthesitis total score. Also Achilles tendon thickness was reported to be affected much more by the height of patients with axSpA in comparison to RA patients and healthy subjects. Age was found to be an independent factor for high enthesitis scores only in the axSpA group.[25]

In a recent cross-sectional study on 50 patients with AS and 30 healthy controls to compare the ultrasonographic findings of entheses in AS patients and controls, bone erosion in the calcaneal enthesis and the plantar fascia, and plantar thickening were statistically more prominent in the AS group.[26] Similarly, the bone profile scores reflecting the erosions were also higher in AS and nr-axSpA patients than controls in our study. In another study to evaluate the validity of enthesis US in the evaluation of disease activity in patients with early SpA, Achilles US examinations were performed at baseline, 6 and 12 months and compared with clinical outcome indices. Unlike our study, the Achilles Doppler signal and US structure alteration were significantly associated with high CRP and ESR levels at baseline and patients who had basal high ASDAS had significantly higher Achilles total US score. As a result, they reported that Doppler US had significant associations with other disease activity measures including ESR, CRP and ASDAS.[27] We also observed positive association between PD US and MASES scores in patients with AS in the current study.

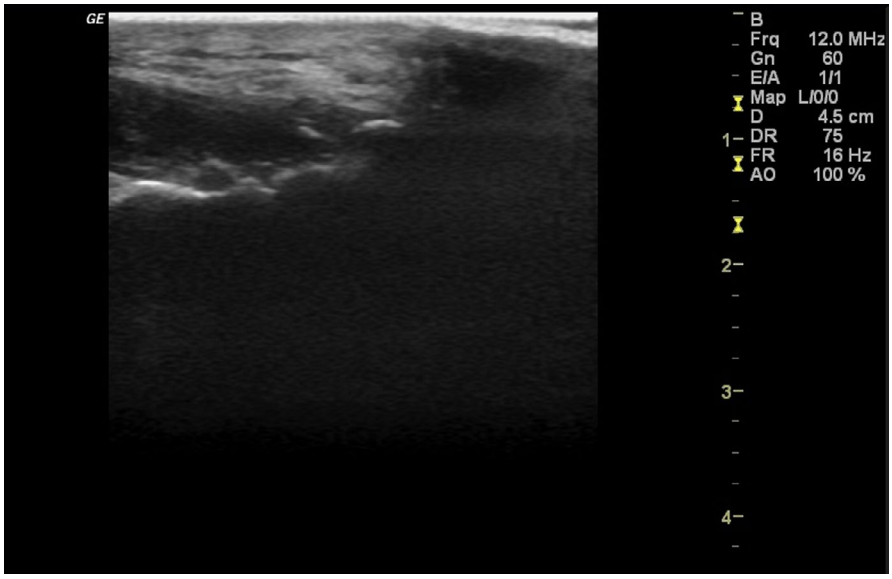


FIGURE 1 Ultrasound findings: enthesophyte

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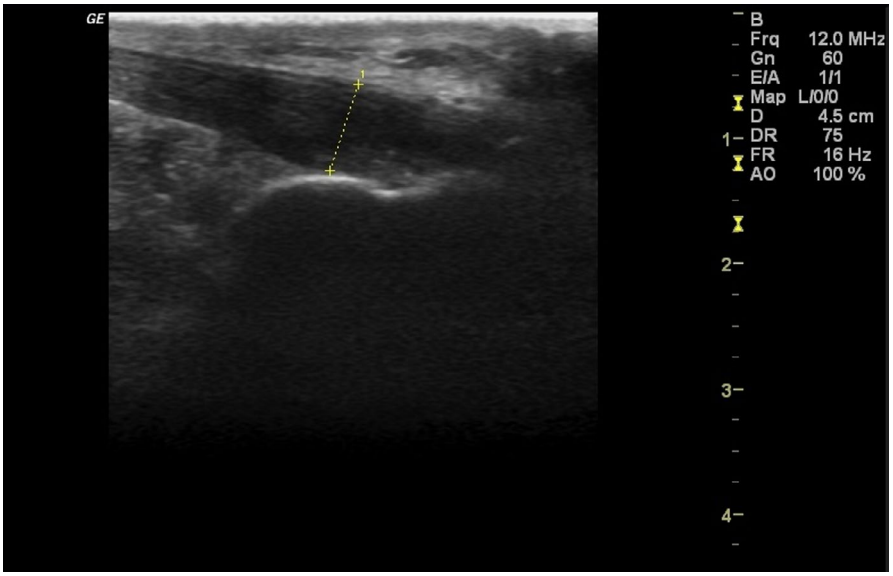


FIGURE 2 Ultrasound findings: tendon thickness

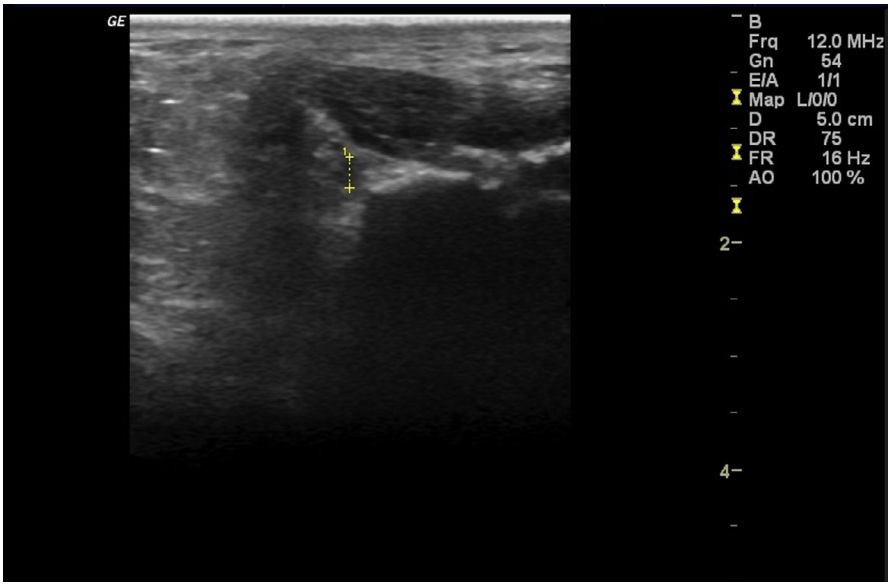


FIGURE 3 Ultrasound findings: retrocalcaneal bursa

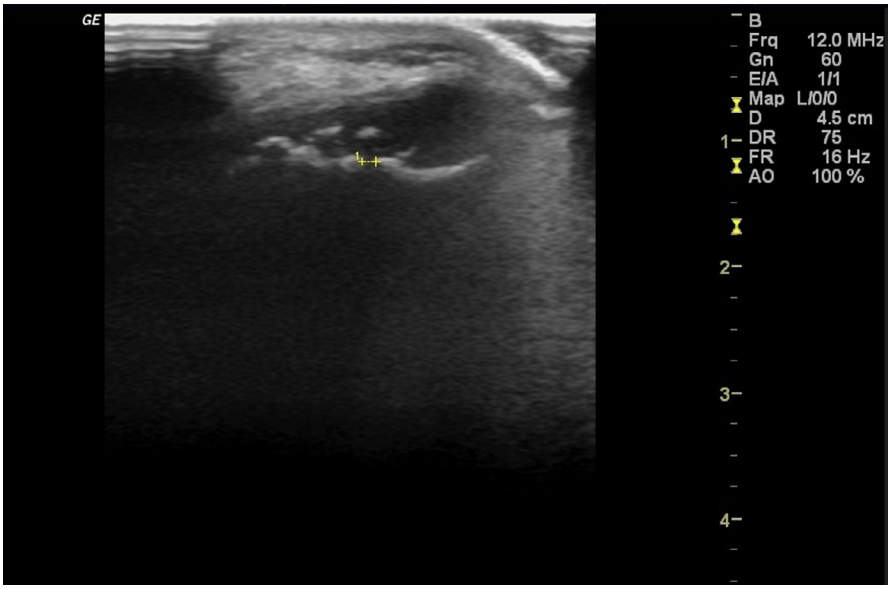


FIGURE 4 Ultrasound findings: bone profile

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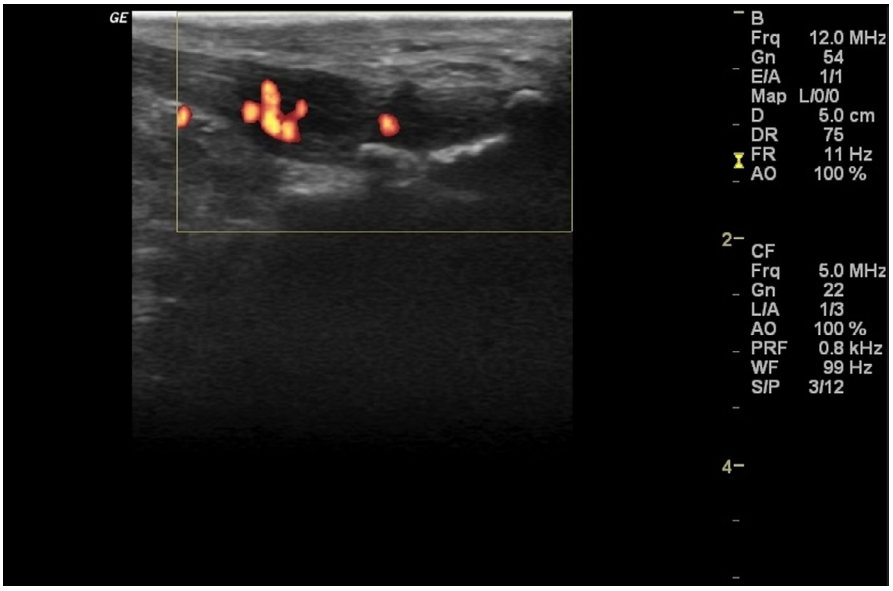


FIGURE 5 Ultrasound findings: enthesitis (Doppler findings)

The main limitation of the current study is lacking an assessment of inter- and intra-reader reliability. Filippucci et al evaluated the Achilles tendon and reported that inter-observer and intra-observer reproducibility and OMERACT staging were reliable.[9] Furthermore, this study included US evaluation of 2 rheumatologists for each patient at the same time. However, it would be better if the same observer had re-evaluated the same patient and intra- and inter-observer evaluations had been performed in this study.

5 | CONCLUSION

In this study, AS and nr-axSpA patients were found to be similar in clinical and functional aspects and US findings. The similarity in HLA-B27 positivity, extra-articular peripheral involvement, disease activity, and ultrasonographic enthesitis scores suggests that these 2 entities are different phenotypic reflections of the same disease spectrum, rather than 2 distinct disorders. The positive correlation between PD and MASES scores in AS patients substantiate the performance of MASES in evaluation of entheseal activity.

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REFERENCES

1. Protopopov M, Poddubnyy D. Radiographic progression in non-radiographic axial spondyloarthritis. *Expert Rev Clin Immu*. 2018;14(6):525-533.
2. Backhaus M, Burmester G-R, Gerber T, et al. Guidelines for musculoskeletal ultrasound in rheumatology. *Ann Rheum Dis*. 2001;60(7):641-649.
3. Wang CH, Feng Y, Ren Z, et al. Performance of ultrasound to monitor Achilles enthesitis in patients with ankylosing spondylitis during TNF-a antagonist therapy. *Clin Rheumatol*. 2015;34(6):1073-1078.
4. Kamel M, Eid H. Ultrasound detection of heel enthesitis: a comparison with magnetic resonance imaging. *J Rheumatol*. 2003;30(4):774-778.
5. van der Linden S, Valkenburg HA. Evaluation of diagnostic criteria for ankylosing spondylitis. A proposal for modification of the New York criteria. *Arthritis Rheum*. 1984;27(4):361-368.
6. Rudwaleit M, Van der Heijde D, et al. The development of Assessment of SpondyloArthritis international Society classification criteria for axial spondyloarthritis (part II): validation and final selection. *Ann Rheum Dis*. 2009;68(6):777-783.
7. Wakefield RJ, Balint PV, Szkudlarek M, et al. Musculoskeletal ultrasound including definitions for ultrasonographic pathology. *J Rheumatol*. 2005;32(12):2485-2487.
8. Aydin SZ, Karadag O, Filippucci E, et al. Monitoring Achilles enthesitis in ankylosing spondylitis during TNF-a antagonist therapy: an ultrasound study. *Rheumatology*. 2010;49:578-582.
9. Filippucci E, Aydin SZ, Karadag O, et al. Reliability of high-resolution ultrasonography in the assessment of Achilles tendon enthesopathy in seronegative spondyloarthropathies. *Ann Rheum Dis*. 2009;68(12):1850-1855.
10. Rumyantseva DG, Dubinina TV, Demina AB, et al. Ankylosing spondylitis and non-radiographic axial spondyloarthritis: two stages of disease? *Ter Arkh*. 2017;89(5):33-37.
11. De Winter JJ, van Mens LJ. Prevalence of peripheral and extra-articular disease in ankylosing spondylitis versus non-radiographic axial spondyloarthritis: a meta-analysis. *Arthritis Res Ther*. 2016;18(1):196.
12. Corli J, Flipo RM, Philippe P, et al. Tumor necrosis factor-alpha inhibition in ankylosing spondylitis and nonradiographic axial spondyloarthritis: treatment response, drug survival, and patient outcome. *J Rheumatol*. 2015;42(12):2376-2382.
13. Malaviya AN, Kalyani A. Comparison of patients with ankylosing spondylitis (AS) and non-radiographic axial spondyloarthritis (nr-axSpA) from a single rheumatology clinic in New Delhi. *Int J Rheum Dis*. 2015;18(7):736-741.
14. Maas F, Spoorenberg A, Brouwer E, et al. Spinal radiographic progression in patients with ankylosing spondylitis treated with TNF-alpha blocking therapy: a prospective longitudinal observational cohort study. *PLoS ONE*. 2015;10(4):e0122693.
15. Kiltz U, Baraliakos X, Karakostas P, et al. Do patients with non-radiographic axial spondylarthritis differ from patients with ankylosing spondylitis? *Arthritis Care Res*. 2012;64(9):1415-1422.

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16. Jeong H, Yoon JY, Park EJ, et al. Clinical characteristics of nonradiographic axial spondyloarthritis in Korea: a comparison with ankylosing spondylitis. *Int J Rheum Dis*. 2015;18(6):661-668.
17. Bakirci S, Dabague J, Eder L, et al. The role of obesity on inflammation and damage in spondyloarthritis: a systematic literature review on body mass index and imaging. *Clin Exp Rheumatol*. 2019.
18. Aydin SZ, Can M, Alibaz-Oner F, et al. A relationship between spinal new bone formation in ankylosing spondylitis and the sonographically determined Achilles tendon enthesophytes. *Rheumatol Int*. 2016;36(3):397-404.
19. Spadaro A, Iagnocco A, Perrotta FM, Modesti M, Scarno A, Valesini G. Clinical and ultrasonography assessment of peripheral enthesitis in ankylosing spondylitis. *Rheumatology*. 2011;50:2080-2086.
20. Baraliakos X, Kiltz U, Appel H, et al. Chronic but not inflammatory changes at the Achilles' tendon differentiate patients with peripheral spondyloarthritis from other diagnoses – Results from a prospective clinical trial. *RMD Open*. 2017;3:e000541.
21. Suleyman E, Nas K. Clinical and ultrasonographic enthesopathy in inflammatory rheumatic diseases: is MASEI or only calcaneal enthesitis sufficient? *Z Rheumatol*. 2018;77(8):719-726.
22. Hamdi W, Chelli-Bouaziz M, Ahmed MS, et al. Correlations among clinical, radiographic, and sonographic scores for enthesitis in ankylosing spondylitis. *Joint Bone Spine*. 2011;78(3):270-274.
23. Ruyssen-Witrand A, Jamard B, Cantagrel A, et al. Relationships between ultrasound enthesitis, disease activity and axial radiographic structural changes in patients with early spondyloarthritis: data from DESIR cohort. *RMD Open*. 2017;3(2):e000482.
24. Palominos PE, de Campos APB, Ribeiro SLE, et al. Correlation of enthesitis indices with disease activity and function in axial and peripheral spondyloarthritis: a cross-sectional study comparing MASES, SPARCC and LEI. *Adv Rheumatol*. 2019;59(1):23.
25. Harman H, Süleyman E. Features of the Achilles tendon, paratenon, and enthesis in inflammatory rheumatic diseases: a clinical and ultrasonographic study. *Z Rheumatol*. 2018;77(6):511-521.
26. Ishida SN, Furtado RNV. Ultrasound of entheses in ankylosing spondylitis patients: the importance of the calcaneal and quadriceps entheses for differentiating patients from healthy individuals. *Clinics*. 2019;74:e727.
27. Falcao S, Castillo-Gallego C, Peiteado D, Branco J, Martín Mola E, de Miguel E. Can we use enthesis ultrasound as an outcome measure of disease activity in spondyloarthritis? A study at the Achilles level. *Rheumatology*. 2015;54:1557-1562.

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