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Original Article

Ultrasonographic evaluation of enthesitis in patients with ankylosing spondylitis

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Abstract

The aim of this study was to assess sensitivity and responsiveness of power Doppler ultrasound (PDUS) in detecting enthesitis for ankylosing spondylitis (AS) patients compared to clinical examinations. Twenty AS patients initiating etanerceptunderwent clinical and PDUS examinations of six bilateral entheseal sites at baseline and after 1, 2 and 3 months of treatment. Clinical and PDUS examinations identified at least one entheseal lesion in nine (45%) and 19 (95%) patients, respectively. Furthermore, of 240 entheseal sites examined in these 20 patients, PDUS detected 123 entheseal lesions (51.3% of sites), compared with only 47 entheseal lesions (19.6%) detected by clinical examination ($P < 0.05$). The entheseal lesions found on PDUS were most commonly identified by calcification (33.3%), tendon edema (29.2%), abnormal blood flow (25.8%), a thickened tendon (22.1%), cortical irregularity (12.9%), bony erosions (9.6%) and bursitis at the tendon insertion to the bone cortex (7.1%). Improvements in clinical symptoms and laboratory parameters, and significant decreases in PDUS scores were observed following treatment with etanercept. Improvements in PDUS scores continued during follow-up in patients who entered remission following treatment. In conclusion, PDUS improves detection of structural and inflammatory abnormalities of the enthesis in AS compared to physical examination. In addition, PDUS may be useful inascertaining medications.

Keywords: power Doppler ultrasound, enthesitis, ankylosing spondylitis

Introduction

Enthesitis is a term used to describe inflammation at the ligaments, tendons, aponeurosis or joint capsule insertions into the bone, which is a characteristic feature of ankylosing spondylitis (AS)[1]. Entheseal lesions are defined as a characteristic sign of spondyloarthritis in several classification criteria, such as the Amor criteria[2], the European Spondyloarthropathy Study Group criteria[3], and the Assessment of Spondyloarthritis International Society classification criteria for axial/peripheral spondyloarthritis[4–5]. Imaging modalities for evaluating entheseal lesions include conventional radiology, bone scintigraphy, magnetic resonance imaging (MRI) and power Doppler (PD) ultrasound (US)[6]. X-rays and computerized tomography (CT) scans are insensitive for entheseal lesions in the early stages, although these modalities can visualize the presence of bony erosions and new bone formation at entheseal sites. MRI is expensive and unable to visualize the normal structure of tendon entheses in routine sequences, despite its ability to identify tendon

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entheseal lesions[7]. US has its own unique advantage in the diagnosis of enthesitis in AS; it uses a high-frequency or ultra-high-frequency probe that effectively visualizes the internal structure of the tendon and is recognized as the gold standard for tendon involvement. US is superior to clinical examination in the detection of peripheral enthesitis. Manifestations of tendon enthesitis in AS on US include a thickened tendon, hypoechoicity, local calcification and bony erosion. Abnormal blood flow in tendon entheseal sites can be detected by PDUS[8].

However, US is infrequently used in the detection of peripheral entheseal lesions in AS patients than in patients with rheumatoid arthritis due to lack of an universal diagnostic criteria. Current scoring criteria for US evaluation of entheseal lesions in patients with AS include the Glasgow US Enthesitis Scoring System (GUESS)[9], the D'Agostino Scoring System[10], the Spanish Enthesitis Index[11] and the Madrid Sonographic Enthesis Index (MASEI)[12]. US evaluation of entheseal lesions in patients with AS is mainly through semi-quantitative analysis. It has been shown that US evaluation of entheseal lesion *via* semi-quantitative scoring facilitates early diagnosis and monitoring of AS. However, no large multicenter clinical trials have yet been conducted. Furthermore, the identification of sites which better predict the occurrence of AS remains unknown.

This study was to identify radiological characteristics of peripheral entheseal involvement in AS via PDUS; to compare PDUS and clinical examinations for detecting entheseal lesions; to further explore drug-response assessments of AS by comparing PDUS obtained before and after medical treatment.

Patients and methods

Twenty consecutive patients with AS were recruited at the Drum Tower Clinical Medical College of Nanjing Medical University. The inclusion criteria were: (1) age above 18 years; (2) disease consistent with the 1984 Modified New York Criteria for AS; (3) active disease with a Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) score of $\geqslant 4$; (4) All patients received etanercept 50 mg subcutaneously once weekly. The exclusion criteria were: (1) concurrent presence of other autoimmune disorders; (2) concurrent presence of severe disorders affecting other systems; (3) in the presence of severe infections, repeated infections, active tuberculosis or active hepatitis; (4) pregnancy or breastfeeding; (5) significant laboratory abnormalities: alanine aminotransferase (ALT) or aspartate aminotransferase (AST) $>$ 1.5 times upper limit of normal (ULN), total bilirubin $>$ ULN, serum creatinine $>$ ULN, platelet count $<$ 100,000/mm^3, hemoglobin $<$ 8.5 g/dL and white blood cells $<$ 3,000/mm^3.

Informed consent was obtained from each patient prior to the study. The study was approved by Ethics Committee of the Drum Tower Clinical Medical College of Nanjing Medical University.

Clinical and PDUS examinations were performed at baseline and at 1, 2 and 3 months after starting etanercept. Clinical examination, including physical examination of entheseal sites, was performed by a single rheumatologist. Clinical enthesitis was considered to be present if the patient was positive for at least one of the following: spontaneous pain, swelling or tenderness of the entheseal site. The patients were divided into the clinically symptomatic and clinically asymptomatic groups based on physical examination findings. The patients were instructed to complete BASDAI and a questionnaire on their general condition. Erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) level and visual analog scale (VAS) as well as VAS physician scores (physician assessment of disease activity) during follow up were obtained for each patient.

Phillips iU22 color Doppler US system with a high-frequency linear-array probe (frequency range 7–12 MHz) was used. Each patient was evaluated for the following six bilateral tendon entheses according to the most commonly used entheseal sites described by the current scoring system[9–12]: insertion of the common extensor tendon to the lateral humeral epicondyle; insertion of the tendon of the gluteus maximus to the greater trochanter of the femur; insertion of the quadriceps tendon of the femur to the superior pole of the patella; distal insertion of the patellar ligament to the tibial tuberosity; insertion of the Achilles tendon to the superior pole of the calcaneus; insertion of the plantar aponeurosis to the inferior pole of the calcaneus.

All entheseal abnormalities were validated on at least two cross sections oriented perpendicular to each other to minimize risk of anisotropic artifacts. The characteristics examined included tendon thickness, calcification within the tendon (ligament), bursitis, bone erosion, osteophytes, and Doppler signals at the entheseal site. Tendon thickness was measured at the thickest part of the tendon. The main manifestations of bursitis included confinement to the physiologic site of the bursa mucosa and a compressible hypoechoic or anechoic area. Bone erosion was defined as the continuous interruption of the bone at the entheseal site. An osteophyte was defined as a hyperechoic projection from the terminal part of the bone surface at the entheseal site. Both calcification within the tendon (ligament) and osteo-

phytes at the entheseal site were marked. The presence of blood flow signals were considered to be positive when PDUS was set at a pulse frequency of 400 Hz and a low-pass filter channel of 20 dB.

Semi-quantitative staging was performed for each entheseal lesion in accordance with the scoring system described by France D'Agostino and colleagues[10]. An overall entheseal lesion score was calculated for each patient based on the entheseal structure, tendon thickness, presence/absence of bone erosion, calcification and bursitis, and Doppler signals. The maximum overall score was 144 points (***Supplementary Table 1***).

Statistical analysis

All analyses were performed using SPSS 18.0. For changes in PDUS score, clinical and laboratory results between different time points, since the data were not normally distributed, we ran a Wilcoxon signed-rank test for statistical analysis. A P value of less than 0.05 was considered statistically significant.

Results

Patient demographics

Twenty AS patients were included in the study. Their age ranged from 18 to 43 years with a disease duration from 1 to 8 years. Six patients had extra-articular manifestations; of whom three patients had anterior uveitis and three had psoriasis. The BASDAI score ranged from 4.1 to 8.1, the patient VAS score ranged from 40 to 90 mm, the physician VAS score ranged from 35 to 75 mm, ESR ranged from 7 to 110 mm/hour and CRP level ranged from 0.2 to 82 mg/L (***Table 1***).

PDUS features of entheses in AS patients

In patients with AS, the pathological tendon was thickened and hypoechoic. The fluid within the bursa mucosa exceeded normal ranges and was accompanied by bursal hyperplasia (i.e., bursitis). Bone irregularities were seen at the tendon enthesis insertion into the bone cortex. Local echoes were deranged and coarse (bone cortex destruction), and solitary or multiple scattered spotty or streak-like hyperechoes were seen at the tendon insertion into the bone cortex (calcification) (***Fig. 1A***). Blood flow signal was detected at the tendon insertion into the bone cortex (***Fig. 1B***)(supplementary video is available online).

Comparison of PDUS and clinical examination of enthuses in AS

At least one entheseal lesion was detected in nine patients (45%, 9/20) by clinical examination and in nineteen patients (95%, 19/20) by PDUS. A total of 240 entheseal sites were examined. ***Table 2*** shows the abnormalities identified at each site. PDUS identified abnormalities at 123 of these sites (51.3%), while clinical examination found abnormalities inonly 47 sites (19.6%; $P < 0.05$ versus US). The tendon entheseal lesions on US included calcification (33.3%), tendon edema (29.2%), abnormal blood flow (25.8%), thickened tendon (22.1%), bone cortical irregularities (12.9%), bone erosion (9.6%) and bursitis (7.1%) at the tendon insertion to the bone cortex.

Semi-quantitative staging was performed for abnormal entheses in accordance with the enthesis scoring criteria developed by D'Agostino (***Table 3***)[7]. Of the 123 abnormal entheses identified by PDUS, blood flow signal was observed in 94 sites (39.2% of the total examined), of which 27 sites were stage 1, 36 were stage 2a and 31 were stage 3a; there was no blood flow signal at 29 sites (12.1%), of which 17 sites were stage 2b and 12 were stage 3b.

Of the 47 entheseal lesions identified by clinical examination, 21 sites (44.7%) were normal and 26

Table 1 **Main clinical characteristics of 20 AS patients.**

Characteristic	Result ($n = 20$)
Male/female, *n*	17/3
Age, years	25.5±9.6
Disease duration, years	4.3±3.1
BASDAI score	5.9±3.7
Extra-articular manifestations, *n* (%)	6 (30)
Patient VAS score, mm	64.5±27.7
Physician VAS score, mm	57.5±24.3
ESR, mm/hour	28±17
CRP, mg/L	21.6±14.8

Data are mean±standard deviation, unless otherwise specified. AS: ankylosing spondylitis; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; VAS: visual analog scale; ESR: erythrocyte sedimentation rate; CRP: C-reactive protein.

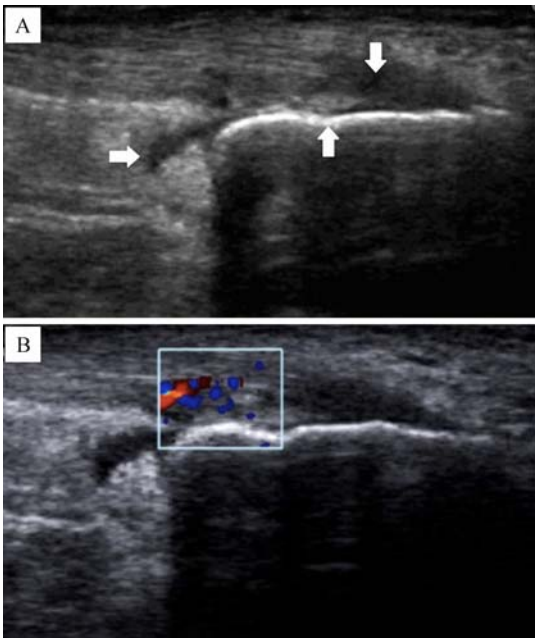

Fig. 1 **Pathological ultrasonographic appearances of Achilles tendon.** In a patient with ankylosing spondylitis, the pathological Achilles tendon is thickened and hypoechoic (↓). The fluid within the bursa mucosa exceeds normal ranges and can be accompanied by bursal hyperplasia (i.e., bursitis →). Bone irregularities are seen at the tendon enthesis insertion into the bone cortex (↑) (A). A blood-flow signal can be detected at the tendon insertion into the exposed bone cortex (B).

(55.3%) were abnormal on PDUS. Blood flow signal was observed in 20 of these 26 sites (42.6% of the original 47 lesions). Of 193 clinically negative entheses, 49.2% were abnormal on PDUS, with abnormal blood flow observed in 40.9% (***Table 4***).

The clinical examination had a sensitivity of 16% and 23%, respectively, for PDUS abnormalities with and without abnormal blood flow, and a specificity of 86% and 85%, respectively, for PDUS abnormalities with and without abnormal blood flow).

PDUS and clinical manifestation before and after etanercept treatment

After etanercept treatment, all twenty AS patients showed improvement in clinical symptoms and laboratory parameters. Significantly decreased disease activity and PDUS scores were also evident (***Fig. 2***). PDUS scores continued to improve during follow-up in patients who achieved remission with treatment (***Table 5***).

Discussion

The incidence of peripheral enthesitis in patients with AS is 25%–58%[13]. Among imaging technologies, musculoskeletal US, including two-dimensional US and PDUS, plays an increasingly important role in the assessment of AS because it can detect subclinical entheseal lesions. Furthermore, PDUS can identify abnormal blood flow within entheseal lesions, which is highly specific for the diagnosis of spondyloarthritis[10]. PDUS has superior sensitivity in detecting enthesitis in AS patients to clinical examination, although there are certain discrepancies between clinical and US examinations. In our study, PDUS detected at least one entheseal lesion in 95% of AS patients compared to 45% of AS patients who were examined clinically. In addition, PDUS detected 51.3% of all entheses to be abnormal compared to 19.6% of all clinically examined sites. These results are consistent with those from previous studies[9–12]. The gold standard for enthesitis diagnosis is histological examination of the corresponding site. In AS, due to difficulties in obtaining entheses samples, there are no studies comparing histological evidence of inflammation and signs of enthesitis assessed with US.

Some US studies have shown that enthesitis is most

Table 2 **PDUS and clinical manifestations of 240 tendon entheses.**

Entheseal abnormality *n* (%)	Site						
	Lateral humeral epicondyle	The greater trochanter	Quadriceps tendon ofthe femur	Tibial tuberosity	Achilles tendon	Plantar aponeurosis	All sites
Calcification	16 (40.0)	30 (75.0)	17 (42.5)	10 (25.0)	3 (7.5)	4 (10.0)	80 (33.3)
Bone erosion	14 (35.0)	3 (7.5)	1 (2.5)	3 (7.5)	2 (5.0)	0	23 (9.6)
Bone irregularity	7 (14.5)	10 (25.0)	2 (5.0)	9 (22.5)	2 (5.0)	1 (2.5)	31 (12.9)
Tendon oedema	20 (50.0)	12 (30.0)	20 (50.0)	9 (22.5)	5 (12.5)	4 (10.0)	70 (29.2)
Thickening	7 (17.5)	6 (15.0)	11 (27.5)	13 (32.5)	11 (27.5)	5 (12.5)	53 (22.1)
Bursitis	0	0	1 (2.5)	5 (12.5)	11 (27.5)	0	17 (7.1)
Power Doppler	12 (30.0)	9 (22.5)	8 (20.0)	12 (30.0)	15 (37.5)	6 (15.0)	62 (25.8)
At least one PDUS abnormality	18 (45.0)	23 (57.5)	24 (60.0)	28 (70.0)	20 (50.0)	10 (25.0)	123 (51.3)
At least one clinical abnormality	7 (17.5)	3 (7.5)	14 (35.0)	7 (17.5)	13 (32.5)	3 (7.5)	47 (19.6)

Table 3 **Staging of 123 abnormal entheseal sites.**

Site	Enthesitis with abnormal blood flow, *n* (%)				Enthesitis without abnormal blood flow, *n* (%)		
	Stage 1	Stage 2a	Stage 3a	Total (1 + 2a + 3a)	Stage 2b	Stage 3b	Total (2b + 3b)
Lateral humeral epicondyle	3 (7.5)	7 (17.5)	2 (5.0)	12 (30.0)	4 (10.0)	2 (5.0)	6 (15.0)
Greater trochanter	5 (12.5)	7 (17.5)	6 (15.0)	18 (45.0)	3 (7.5)	2 (5.0)	5 (12.5)
Quadriceps tendon of the femur	8 (20.0)	6 (15.0)	6 (15.0)	20 (50.0)	4 (10.0)	0	4 (10.0)
Tibial tuberosity	6 (15.0)	5 (12.5)	9 (22.5)	20 (50.0)	7 (17.5)	1 (2.5)	8 (20.0)
Achilles tendon	3 (7.5)	7 (17.5)	5 (12.5)	15 (37.5)	2 (5.0)	2 (5.0)	5 (12.5)
Plantar aponeurosis	2 (5.0)	4 (10.0)	3 (7.5)	9 (22.5)	1 (2.5)	1 (2.5)	1 (2.5)
All sites	27 (11.3)	36 (15.0)	31 (12.9)	94 (39.2)	17 (7.1)	12 (5)	29 (12.1)

Table 4 **Comparison of PDUS and clinical examination of entheses.**

Site	Clinically positive enthesitis (*n* = 47), *n* (%)			Clinically negative enthesitis (*n* = 193), *n* (%)		
	Normal US	US with abnormal blood flow	US without abnormal blood flow	Normal US	US with abnormal blood flow	US without abnormal blood flow
Lateral humeral epicondyle	2 (28.6)	4 (57.1)	1 (14.3)	14 (41.2)	14 (41.2)	6 (17.6)
Greater trochanter	0	2 (66.7)	1 (33.3)	15 (48.4)	16 (51.6)	0
Quadriceps tendon of the femur	6 (42.9)	5 (35.7)	3 (21.4)	13 (36.1)	20 (55.6)	3 (8.3)
Tibial tuberosity	2 (28.6)	5 (71.4)	0	19 (54.3)	13 (37.1)	3 (8.6)
Achilles tendon	9 (69.2)	3 (23.1)	1 (7.7)	17 (60.7)	7 (25.0)	4 (14.3)
Plantar aponeurosis	2 (66.7)	1 (33.3)	0	20 (69.0)	9 (31.0)	0
All sites	21 (44.7)	20 (42.6)	6 (12.8)	98 (50.8)	79 (40.9)	16 (8.3)

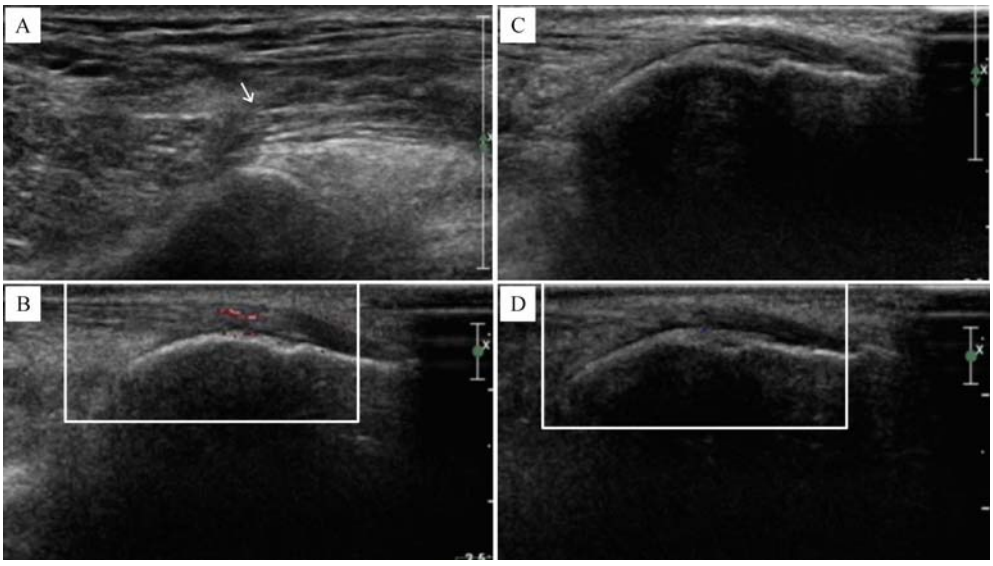

Fig. 2 **Ultrasonographic appearances of Achilles tendon before and after treatment in a patient with AS.** The Achilles tendon is not clear and hypoechoic (A, arrow), with a blood flow signal (B) before treatment. After three months of etanercept treatment, the ultrasonographic appearances reveals improvements in tendon structure (C) and blood flow (D).

Table 5 **PDUS scores and clinical parameters at baseline and after medical treatment**

Index/parameter	Baseline	Time post treatment		
		1 month	2 months	3 months
PDUS score	106 (77–136)	74 (51–89)**	51 (35–81)*	37 (29–63)*
BASDAI score	5.8 (4.1–8.0)	4.0 (3.2–7.0)**	2.8 (1.7–3.6)*	2.1 (0.9–2.8)
Patient VAS score	65 (45–88)	39 (35–60)**	27 (25–40)*	20 (10–28)
Physician VAS score	57 (35–75)	23 (14–35)**	15 (6–27)	11 (2–45)
ESR (mm/h)	28 (7–110)	13 (4–23)**	15 (2–43)	15 (5–77)
CRP (mg/L)	21 (0.2–82)	2 (0.2–21)**	3 (0.2–26)	3 (0.2–30)

Data are median (range). Wilcoxon signed-rank test was used to compare baseline *vs*. 1 month, 1 month *vs*. 2 months, and 2 months *vs*. 3 months. *$P < 0.05$; **$P < 0.01$, $n = 20$

commonly distributed in the distal portion of the lower extremities in patients of AS. In a study by D'Agostino involving 164 spondyloarthritis patients (including 104 AS patients), at least one entheseal lesion was detected on PDUS in 161 patients. The most commonly affected sites were the distal entheses of the lower extremities, such as the Achilles tendon, plantar fascia and patellar tendon, which had an incidence in AS patients of 79%, 74% and 59%, respectively[10]. In the study by Kiris *et al.* involving 30 AS patients, more entheseal lesions of the lower extremities were observed when two-dimensional US was combined with PD[14]. It remains unclear why enthesitis is most commonly distributed in the distal portion of the lower extremities, but this might be closely related to anatomical structure and mechanical factors; for example, the size of the Achilles tendon is larger than other tendons. In normal-aged entheses and in spondyloarthritis-related enthesitis, McGonagle *et al.* found that erosion and new bone formation occurred at different topographical locations, with new bone typically forming at the distal part of the enthesis where the bone is under more tension, strongly suggesting a role for mechanical factors in physiologic and pathological enthesis remodeling in humans[15]. Therefore, biologic mechanical stress may play an important role in the pathogenesis of inflammatory and mechanical entheseal lesions, and this mechanical action can be scaled up in spondyloarthritis, especially in HLA-B27-positive patients[16].

However, a high incidence of entheseal lesions is also observed in the upper limbs. Our study detected 45% of entheses of the lateral humeral epicondyle, which indicates that other mechanisms, beyond biomechanical factors, might be involved in pathogenesis of spondyloarthritis-related enthesitis. Moreover, our study showed that tendon enthesis abnormalities most commonly found on US were calcification (33.3%), low-level echo (29.2%) and a thickened tendon (22.1%) at the tendon insertion to the bone cortex. These findings, however, are not specific to entheseal lesions in AS. On the other hand, the incidence of bone erosion, which is highly indicative of AS, was only 9.6%.

A prospective study of 60 AS patients found that US had excellent sensitivity for erosions, swelling and new bone formation, but very poor specificity compared with radiographs[17]. Negative and positive predictive outcomes were good only for erosion. The authors concluded that US seems to be a useful instrument in detecting signs of chronic enthesitis in AS, particularly when radiographs are normal. These findings are consistent with our study. In addition, in our study, the incidence of a PD signal at the tendon enthesis was higher than that reported in other comparable studies[9]. This may be due to most of patients enrolled in our study were treatment-naïve AS patients with high disease activity indices.

In our study, interestingly enough, significant inconsistency was observed in detecting tendon enthesitis between PDUS and clinical examination. This can be explained by the fact that some entheseal lesions are subclinical in nature, and US can detect more of these subclinical lesions than clinical examination[9–10]. On the other hand, among the entheseal lesions identified by clinical examination, 44.7% were normal on US, which is consistent with the results from some previous studies. Because eight patients with peripheral joint involvement were enrolled in our study, enthesitis by clinical examinations might be caused by peripheral arthritis, which may increase the chance of false positive enthesitis observed in clinical examinations. In other words, there is an inconsistency in detectingentheseal lesions between clinical examination and US.

Quantification of disease still remains an important aspect in the management of AS, both for activity and structural damage. For this purpose, scoring systems are relevant for monitoring changes. US is still used less frequently in AS than in rheumatoid arthritis. The lack of universal diagnostic criteria is considered to be an

important reason for this. Some of the commonly used diagnostic criteria are GUESS[9] and MASEI[12,18]. GUESS is mainly intended for evaluating the main entheses of the lower extremities. US results in spondyloarthritis patients under this system have indicated that clinical examination has a lower sensitivity (22.6%) but higher specificity (79.7%) compared with US. However, no correlation was seen between the scores of entheseal sites based on US results and ESR and CRP[9]. This may be caused by the fact that only main entheses of the lower extremities are included in this scoring system, thus failing to comprehensively reflect the overall condition of spondyloarthritis patients. In one study evaluating sacroiliac joint and lower extremity entheses of 161 AS patients, the BASDAI score had a higher association with color Doppler flow in the sacroiliac joint than in peripheral entheses[19]. Furthermore, there is lack of assessment of inflammation-related color Doppler signals in the GUESS scoring system, which might also be responsible for this system's inability to comprehensively reflect a patient's medical condition.

In contrast, the MASEI includes color Doppler flow signals in its assessment system, apart from coverage of the triceps tendon of the upper extremities[20]. In a controlled study that compared 113 early spondyloarthritis patients with 57 patients with non-inflammatory arthritis, significant intergroup differences were seen in the MASEI score[18]. In another study that compared 25 AS patients with 29 healthy subjects using MASEI, a score of $\geqslant 18$ was highly sensitive and specific for diagnosing spondyloarthritis[12]. The studies available indicate that semi-quantitative analysis is able to detect and diagnose entheseal lesions at an early stage. The scoring method used in our study was mainly derived from MASEI. We have added a pair of tendon entheses inserting them to the greater trochanter of the femur and removing the pair of proximal patellar ligament entheses, taking account of the incidence of clinical peripheral enthesitis, and the convenience of ultrasound operation in some entheseal sites. Of course, future studies with a larger sample size and long-term follow-up are required to scrupulously validate this method.

Until now, the treatment options for AS were limited. Thus, in the past, no attempts were made to search for an objective tool that might evaluate treatment response. In our study, improvements in clinical symptoms and laboratory parameters, as well as significant decreases in PDUS scores, were observed following treatment with etanercept. Improvements in PDUS scores continued during follow-up in patients who entered remission following treatment, which indicates the potential of this modality in monitoring the response to medical therapy. To date, there is only limited literature available with respect to monitoring the efficacy of biologic agents in AS through US. In previous studies, US has been mainly used to monitor improvements in entheseal and joint lesions. According to one set of clinical data, significant improvements in US results, rash, and histological findings were seen after 2 months' treatment with etanercept in patients with psoriasis[21]. Another study evaluating Achilles tendon in spondyloarthritis patients, using US, reported significant decreases in the US score and significant improvements in the BASDAI score, ESR and CRP level after the use of biologic agents[22]. In the study by Naredo *et al.*[23], patients with active spondyloarthritis who were treated with biologic agents were followed for 6 months, PDUS results revealed significant improvements in tendon blood flow, peri-tendon blood flow and bursitis at 6 months. However, no improvements in calcification or bone-surface morphology were observed. A recent study also reported that tumor necrosis factor-α antagonists were effective in decreasing US signs of enthesitis after 3 months of therapy in 100 AS patients[24]. The authors concluded that PDUS is a reliable method for monitoring therapeutic response to tumor necrosis factor antagonists in AS patients with enthesitis of Achilles tendon.

In conclusion, this preliminary self-controlled study demonstrated that PDUS can improve detection of structural and inflammatory abnormalities of enthesis in AS. Its efficacy in providing better evaluation of enthesitis compared to physical examination is more evident. PDUS can be useful inguiding clinical medications. However, one limitation of our study is its relatively small sample size. Thus, future studies with a larger sample size and long-term follow-up is required to further verify the results of this study.

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