

# Echotexture Analysis of L4 Supraspinous Entesis in Ankylosing Spondylitis

CME Credits

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## Abstract

**Background:** Enthesopathy is a main characteristic of ankylosing spondylitis (AS). However, ultrasonographic features of supraspinous entesis in AS have not yet been reported. **Methods:** Forty-seven AS patients and 22 healthy individuals were enrolled and completed the study. L4 supraspinous enteses were assessed through an ultrasound (US) unit with the participants in a lateral decubitus position. Enteseal echogenicity was interpreted upon inspection of the US image. An enteseal grayscale (GS) value determination, along with an echotexture analysis using a gray-level co-occurrence matrix algorithm, was performed. The thoracolumbar fascia just above the entesis was also analyzed. An entesis-to-fascia ratio (EFR) of each texture feature was used for the purpose of intergroup comparison. **Results:** The prevalence of abnormal enteseal echogenicity in the AS and healthy groups was 19.1% and 13.6%, respectively ( $P = 0.42$ ). The AS group experienced a higher GS EFR (0.56 [0.10–1.08] vs. 0.40 [0.12–0.89],  $P = 0.007$ ), higher contrast EFR (0.62 [0.15–1.23] vs. 0.49 [0.23–1.33],  $P = 0.049$ ), higher variance EFR (0.44 [0.06–1.21] vs. 0.35 [0.13–1.10],  $P = 0.023$ ), and lower homogeneity EFR (1.07 [0.97–1.27] vs. 1.11 [1.04–1.19],  $P = 0.011$ ) in comparison to the healthy group. **Conclusion:** Echotexture analysis identified the subtle structural changes in L4 supraspinous entesis in AS patients. It proved to be superior to the inspection method and may possess the potential for providing early detection of supraspinous enthesopathy in AS.

**Keywords:** Ankylosing spondylitis, echotexture analysis, enthesopathy, supraspinous entesis, ultrasonography

## INTRODUCTION

Ankylosing spondylitis (AS) is an inflammatory disease that involves the axial skeletal system, with a characteristic initial manifestation of sacroiliitis. Entesitis, an inflammation of the bony insertion of a tendon, is pathognomonic in AS.<sup>[1]</sup> Peripheral joint entesitis, e.g., Achilles and patellar entesitis, had been well studied.<sup>[2–4]</sup> The ultrasonographic features of entesitis include an increase in thickness, a decrease in echogenicity, and the presence of bone erosion and enthesophytes. In active cases, power Doppler signals on entesis can be seen.<sup>[5]</sup> The supraspinous ligament is anatomically adjacent to the spine and has the potential to be approached by ultrasonography. Its enteseal parts overlying the spinal process, namely the supraspinous enteses, are items within the clinical entesitis scoring system, e.g., the L5

supraspinous entesis for Maastricht Ankylosing Spondylitis Entesitis Score.<sup>[6]</sup> However, no ultrasonographic study on supraspinous entesis has yet been reported. In this study, we use echotexture analysis for ultrasound (US) imaging of supraspinous entesis in AS patients. The aim was to uncover the echotexture features of AS and to clarify the role of image analysis in AS diagnosis.

## PATIENTS AND METHODS

### Patients

This prospective cross-sectional study was approved by our Institutional Review Board (Protocol number: CE16133A).

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Informed consent was obtained from all patients who were enrolled in this study. From September 1, 2016, to December 31, 2017, 56 adult AS patients fulfilling the 1984 modified New York criteria, along with 23 age- and gender-matched healthy adult individuals, were enrolled at the Taichung Veterans General Hospital's Rheumatology outpatient department. AS patients should have had their disease stabilized, when being kept on a stable dose of regular medication for at least 3 months prior to enrollment. All participants received a US assessment for the 4<sup>th</sup> lumbar (L4) supraspinous enthesis on their day of enrollment. For AS patients, information regarding body metrics, disease duration, human leukocyte antigen (HLA)-B27, erythrocyte sediment rate (ESR), C-reactive protein (CRP), and radiographic grading of sacroiliitis was obtained from medical records. Each patient's ESR and CRP levels must be measured within 2 weeks of the day of enrollment. The radiographic grading of sacroiliitis adopted the grade of the poorer side of the sacroiliac joints. The questionnaires of the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Bath Ankylosing Spondylitis Functional Index (BASFI), and Patient Global Assessment (PGA; range, 0–10) were taken on the day of enrolment.<sup>[7,8]</sup> The AS disease activity score (ASDAS)-CRP was subsequently calculated.<sup>[9]</sup>

US image acquisition: A US machine (General Electric LOGIQ e, Milwaukee, Wisconsin, USA) equipped with a 12 MHz linear probe was implemented. Participants were placed in a lateral decubitus position on a bed, with a mild flexion of their lumbar spine, in order to straighten the supraspinous ligament and avoid anisotropy. The first step in US scanning is to find the location of the L4 spinal process. The L4 spinal process is located at the midpoint of the line which connects the bilateral iliac crest. We manually palpated the L4 spinal process and then went inferiorly to the L5 spinal process. Gel was applied to the skin along the L4, L5, and sacral areas. The probe was placed over the skin with a layer of gel between the probe and the skin. We subsequently took a longitudinal scan from the midline of the sacrum, with the probe moving superiorly through to the L5 and then the L4 spinal processes, to reconfirm the location of the L4 spinal process. The bony cortex of the L4 spinal process should be well visualized. The US beam should be perpendicular to the supraspinous ligament fibers. We recorded the grayscale (GS) longitudinal image of the L4 supraspinous enthesis in digital form. A rheumatologist (Lai KL) with 12 years of US experience performed the US assessments. The sonographer was blind to the participants' clinical data prior to the US assessment.

### Traditional ultrasound image interpretation

The thickness of the L4 supraspinous enthesis was measured using the calibration function of the US machine. This thickness measurement was performed at the midpoint of the spinal process bony cortex. The echogenicity of the L4 supraspinous enthesis was compared to the nonentheseal part of the same ligament through use of the inspection method. It would be classified as hypoechoic, isoechoic, or hyperechoic if the brightness of

the entheseal part was less than, the same as, or greater than the brightness of the nonentheseal part, respectively [Figure 1].

To test the intraobserver correlation, each digitally stored US image was then re-read 1 month later. To test the interobserver correlation, the digitally stored US images were reviewed by a separate rheumatologist (Tseng CW), who has 6 years of US experience and was blind to the participants' clinical data.

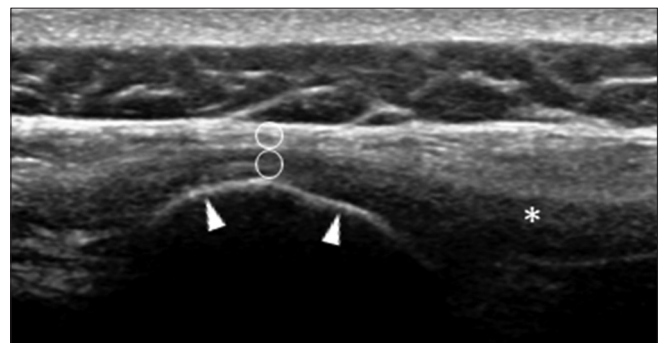
### Echotexture analysis

Image processing should be done before echotexture analysis is performed. The digitalized US image files were opened using Microsoft Paint. Subsequently, we circled the region of interest (ROI) in both the enthesis and overlying thoracolumbar fascia using a solid white line. After circling the ROI, the images were saved as 24-bit bitmap files [Figure 1].

The GS value determination and echotexture analysis were performed using MATLAB R2017b software. The bitmap image files were read in a MATLAB environment. The mean GS values of the ROI for the L4 supraspinous enthesis and thoracolumbar fascia were determined, respectively. The echotextures of the ROI for the L4 supraspinous enthesis and thoracolumbar fascia were analyzed, respectively, using the gray-level co-occurrence matrix (GLCM) algorithm. The angular displacement was set at 0 degrees. GLCM features used in this study included contrast (CON), energy (ENR), homogeneity (HOM), and variance (VAR). The CON returns a measure of intensity CON between a pixel and its neighbor over the complete image (Equation 1). The ENR returns the sum of squared elements in the GLCM (Equation 2). The HOM returns a value that measures the closeness of the distribution of elements in the GLCM to the GLCM diagonal (Equation 3).

The mathematical definitions of the GLCM features are listed as follows:<sup>[10]</sup>

$$CON = \sum_{i=0}^{n-1} \sum_{j=0}^{n-1} G(i, j) (i - j)^2 \quad (1)$$



**Figure 1:** Grayscale longitudinal ultrasound imaging of L4 spinal process in a healthy subject. Bony cortex of spinal process (arrowheads). The thoracolumbar fascia (upper circle), the entheseal part of the supraspinous ligament (lower circle), and the nonentheseal part of the supraspinous ligament (\*). Typically, the enthesis echogenicity is similar to that of the nonentheseal part. Instead, the thoracolumbar fascia is a constantly hyperechoic band structure

$$ENR = \sum_{i=0}^{n-1} \sum_{j=0}^{n-1} G(i, j)^2 \quad (2)$$

$$HOM = \sum_{i=0}^{n-1} \sum_{j=0}^{n-1} G(i, j) / (1 + |i - j|) \quad (3)$$

The co-occurrence matrix  $G(i, j)$  calculates the co-occurrence of the pixels with the values  $i$  and  $j$ , where  $n$  is the number of gray levels of the image.

$$g(i, j) = G(i, j) / \sum_{i=0}^{n-1} \sum_{j=0}^{n-1} G(i, j) \quad (4)$$

$$u = \sum_{i=0}^{n-1} \sum_{j=0}^{n-1} i \cdot g(i, j) \quad (5)$$

$$VAR = \sum_{i=0}^{n-1} \sum_{j=0}^{n-1} (i - u)^2 g(i, j) \quad (6)$$

Here,  $g(i, j)$  is the  $(i, j)^{th}$  entry in the gray-level co-occurrence matrix (Equation 4), and  $u$  is the mean of  $g(i, j)$  (Equation 5). The VAR feature is defined as Equation 6.<sup>[11]</sup>

To overcome the errors of enthesis echogenicity caused by the US machine's settings and the skin thickness among different persons, we adopted an enthesis-to-fascia ratio (EFR) in order to eliminate these errors. For example, the GS EFR was calculated with the mean GS values of the ROI for the L4 supraspinous enthesis and thoracolumbar fascia. The enthesal GS value divided by the thoracolumbar fascial GS value equals the GS EFR. The thoracolumbar fascia is not affected by the disease, so it can be a standard. We used the EFR of the GS value and GLCM features (e.g., GS EFR, CON EFR, ENR EFR, HOM EFR, and VAR EFR) for the purpose of intergroup comparison.

### Statistical analysis

All statistical analyses were computed using the Statistical Package for the Social Sciences (SPSS), Windows Version 18.0 (SPSS Inc., Chicago, Illinois, USA). Quantitative variables were expressed as the mean  $\pm$  standard deviation, and for nonnormally distributed data, as the median (range), and compared using the Mann-Whitney  $U$  test. Qualitative variables were compared using Chi-squared tests and the Fisher's exact test, when appropriate. All statistical analyses were two-tailed, with  $P < 0.05$  considered statistically significant. The correlation between the two quantitative variables was calculated using the Pearson's correlation test. Interobserver and intraobserver correlations were assessed using the kappa statistic. The sensitivity (SEN) and specificity (SPE) of the diagnostic thresholds of the GLCM features were determined through use of the receiver operating characteristic (ROC) curve.

## RESULTS

### Demographic features

Forty-seven AS patients and 22 healthy individuals completed the study, each providing fully available data for analysis. None of participants had local tenderness or swelling at the lumbar spinal processes. The AS patients had a mean age of  $41.0 \pm 14.1$  years, were male predominant (76.6%), had a disease duration of 3.0 (range, 0.2–11.5) years, a high HLA-B27 positivity rate (97.9%), an ASDAS-CRP of 2.0 (range, 0.8–4.6), BASDAI of 3.0 (range, 0.2–8.7), BASFI of 0.8 (range, 0–8.0), and a PGA of 3.5 (range, 1–10). The ESR and CRP were 10 (range, 1–92) mm/h and 0.35 (range, 0.01–8.55) mg/dL, respectively. The distribution of radiographic sacroiliitis was Grade 1 ( $n = 2$ , 4.3%), Grade 2 ( $n = 12$ , 25.5%), Grade 3 ( $n = 17$ , 36.2%), and Grade 4 ( $n = 16$ , 34.0%). The body metrics of the AS patients were height  $166.5 \pm 8.9$  cm, weight  $67.8 \pm 14.7$  Kg, and body mass index  $24.4 \pm 4.6$ . The mean age, male ratio, and body metrics of the healthy individuals were similar to those in the AS group [Table 1].

### Ultrasound findings and echotexture analysis

The thickness of the L4 supraspinous enthesis in the AS patients and healthy individuals was 2.4 (range, 0.3–4.3) mm versus 2.2 (range, 0.7–4.0) mm, respectively ( $P = 0.69$ ). Abnormal enthesis echogenicity, as interpreted by inspection, was present in 19.1% of the AS patients and 13.6% of the healthy individuals ( $P = 0.42$ ). The results of echotexture analysis in the AS and healthy groups were as follows: GS EFR, 0.56 (range, 0.10–1.08) versus 0.40 (range, 0.12–0.89) ( $P = 0.007$ ); CON EFR, 0.62 (range, 0.15–1.23) versus 0.49 (range, 0.23–1.33) ( $P = 0.049$ ); ENR EFR, 1.73 (range, 0.64–5.60) vs. 2.22 (range, 1.39–4.02) ( $P = 0.056$ ); HOM EFR, 1.07 (range, 0.97–1.27) versus 1.11 (range, 1.04–1.19) ( $P = 0.011$ ); and VAR EFR, 0.44 (range, 0.06–1.21) versus 0.35 (range, 0.13–1.10) ( $P = 0.023$ ). Through defining a composite index as the sum of GS EFR, CON EFR, and VAR EFR, the results were 1.65 (range, 0.41–3.33) versus 1.16 (range, 0.54–3.32) ( $P = 0.015$ ) in the AS and healthy groups, respectively [Table 2]. Using plot box statistics, the AS group had a higher median value of GS EFR, CON EFR, and VAR EFR, but exhibited a wider range of these features [Figure 2]. We also grouped the AS patients into low-grade (Grade 1–2) and high-grade (Grade 3–4) sacroiliitis patients. The L4 supraspinous enthesis thickness, echogenicity, GS EFR, CON EFR, ENR EFR, HOM EFR, and VAR EFR did not experience significant differences between the low-grade and high-grade sacroiliitis patients [Table 2].

### Diagnostic values of gray-level co-occurrence matrix features

While using a criterion of abnormal supraspinous enthesis echogenicity for AS diagnosis, the SEN, SPE, positive predictive value (PPV), and negative predictive value (NPV) were 19.1%, 86.4%, 75.0%, and 33.3%, respectively. For GLCM feature EFRs, the cutoff values for AS diagnosis

**Table 1: Demographic data of ankylosing spondylitis patients and healthy controls**

	AS (n=47)	HC (n=22)	P
Male, n (%)	36 (76.6)	19 (86.4)	0.27
Age (years)	41.0±14.1 (20-77)	42.2±6.5 (24-53)	0.70
Body height (cm)	166.5±8.9 (149-191)	171.1±9.8 (151.5-186)	0.09
Body weight (kg)	67.8±14.7 (46.1-116)	73.0±11.8 (46.9-95)	0.15
Body mass index	24.4±4.6 (16.0-39.4)	24.6±2.6 (20.4-30.0)	0.80
Disease duration (years)	3.0 (0.2-11.5)	N/A	
HLA-B27 positive, n (%)	46 (97.9)	N/A	
ESR (mm/h)	10 (1-92)	N/A	
CRP (mg/dL)	0.35 (0.01-8.55)	N/A	
ASDAS-CRP	2.0 (0.8-4.6)	N/A	
BASDAI	3.0 (0.2-8.7)	N/A	
BASFI	0.8 (0-8.0)	N/A	
PGA (0-10)	3.5 (1-10)	N/A	
Radiographic sacroiliitis*, n (%)		N/A	
Grade 1	2 (4.3)		
Grade 2	12 (25.5)		
Grade 3	17 (36.2)		
Grade 4	16 (34.0)		

Quantitative variables were presented as mean±SD (range), and for nonnormally distributed data, as median (range). Qualitative variables were presented as a case n (%). \*Grading sacroiliitis at the poorer side of the sacroiliac joints based on X-ray imaging. AS: Ankylosing spondylitis, HC: Healthy control, HLA: Human leukocyte antigen, ESR: Erythrocyte sedimentation rate, CRP: C-reactive protein, ASDAS: Ankylosing spondylitis disease activity score, BASDAI: Bath ankylosing spondylitis disease activity index, BASFI: Bath ankylosing spondylitis functional index, PGA: Patient global assessment using 0-10 visual analog scale, N/A: Not applicable, SD: Standard deviation

**Table 2: Ultrasound image analysis for L4 supraspinous enthesis**

	AS (n=47)			HC (n=22)	P (sacroiliitis grade 1-2 vs. sacroiliitis Grade 3-4)	P (AS all vs. HC)
	Sacroiliitis Grade 1-2 (n=14)	Sacroiliitis Grade 3-4 (n=33)	All			
Thickness (mm)	2.6 (0.3-4.3)	2.1 (0.8-4.2)	2.4 (0.3-4.3)	2.2 (0.7-4.0)	0.26	0.69
Echogenicity*, n (%)						
Hypoechoic	5 (35.7)	4 (12.1)	9 (19.1)	3 (13.6)	0.13	0.42
Isoechoic	9 (64.3)	29 (87.9)	38 (80.9)	19 (86.4)		
Hyperechoic	0 (0)	0 (0)	0 (0)	0 (0)		
Grayscale EFR	0.49 (0.12-1.08)	0.59 (0.10-1.07)	0.56 (0.10-1.08)	0.40 (0.12-0.89)	0.21	0.007
GLCM features <sup>‡</sup>						
CON EFR	0.59 (0.16-1.20)	0.63 (0.15-1.23)	0.62 (0.15-1.23)	0.49 (0.23-1.33)	0.32	0.049
ENR EFR	2.03 (0.88-5.60)	1.64 (0.64-3.29)	1.73 (0.64-5.60)	2.22 (1.39-4.02)	0.09	0.056
HOM EFR	1.08 (0.98-1.27)	1.07 (0.97-1.16)	1.07 (0.97-1.27)	1.11 (1.04-1.19)	0.22	0.011
VAR EFR	0.37 (0.11-1.18)	0.51 (0.06-1.21)	0.44 (0.06-1.21)	0.35 (0.13-1.10)	0.15	0.023
Composite index <sup>†</sup>	1.41 (0.41-3.33)	1.87 (0.53-3.31)	1.65 (0.41-3.33)	1.16 (0.54-3.32)	0.20	0.015

Quantitative variables were presented as median (range). Qualitative variables were presented as a case n (%). \*Enthesis echogenicity was determined by the inspection method, <sup>‡</sup>Each enthesal GLCM feature was divided by the corresponding fascial GLCM feature and was presented as an EFR, <sup>†</sup>Composite index=Grayscale EFR + CON EFR + VAR EFR. GLCM: Gray-level co-occurrence matrix, AS: Ankylosing spondylitis, HC: Healthy control, CON: Contrast, ENR: Energy, HOM: Homogeneity, VAR: Variance, EFR: Enthesis-to-fascia ratio

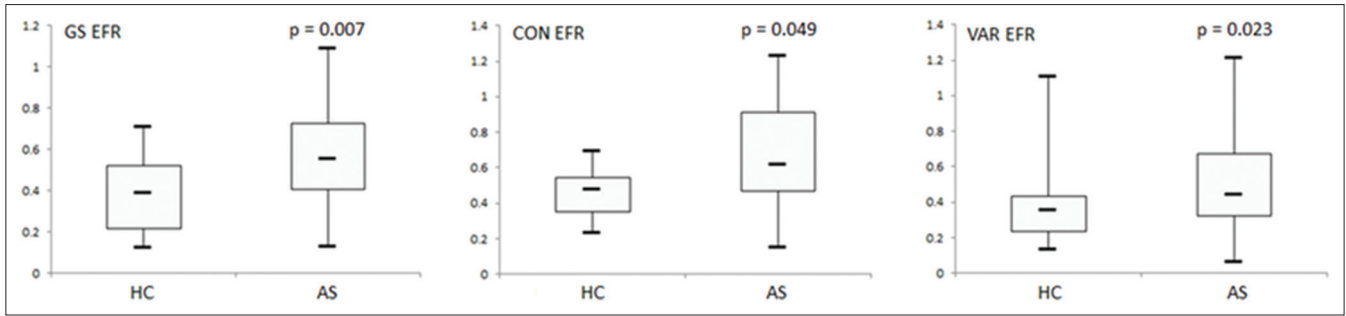
were determined by the ROC curve. With a cutoff value of GS EFR  $\geq 0.71$ , the SEN, SPE, PPV, and NPV were 29.8%, 95.5%, 93.3%, and 38.9%, respectively. With a cutoff value of CON EFR  $\geq 1.02$ , the SEN, SPE, PPV, and NPV were 14.9%, 95.5%, 85.7%, and 33.9%, respectively. With a cutoff value of VAR EFR  $\geq 0.71$ , the SEN, SPE, PPV, and NPV were 25.5%, 95.5%, 91.7%, and 36.8%, respectively. With a cutoff value of the composite index  $\geq 2.06$ , the SEN, SPE, PPV, and NPV were 31.9%, 95.5%, 93.3%, and 38.9%, respectively [Table 3]. The

area under the ROC curve (AUC) was 0.70 for GS EFR, 0.66 for CON EFR, 0.64 for VAR EFR, and 0.67 for the composite index [Figure 3]. The Pearson's correlation coefficients between the disease activity indices and the GLCM features were low in the AS patients [Table 4].

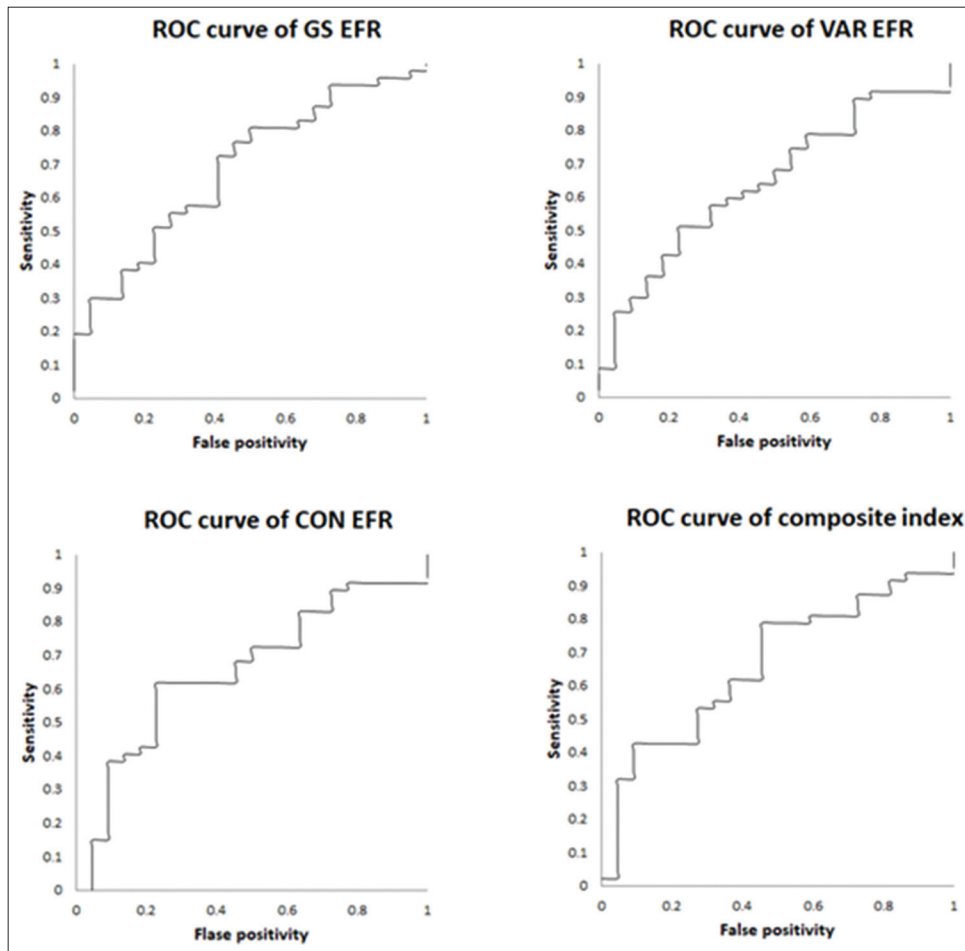
#### Intraobserver and interobserver correlations

The intraobserver and interobserver correlations for L4 supraspinous enthesis echogenicity were excellent (kappa = 0.92 and 0.81, respectively).





**Figure 2:** The plot box of echotextures of L4 supraspinous enthesis. The ankylosing spondylitis group had a higher median value of grayscale enthesis-to-fascia ratio, contrast enthesis-to-fascia ratio, and variance enthesis-to-fascia ratio, but with a wider range of these features. GS: Grayscale; CON: Contrast; VAR: Variance; EFR: Enthsis-to-fascia ratio; HC: Healthy control; AS: Ankylosing spondylitis



**Figure 3:** The receiver operating characteristic curve of the echotexture features. The area under the receiver operating characteristic curve was 0.70 for grayscale enthesis-to-fascia ratio, 0.66 for contrast enthesis-to-fascia ratio, 0.64 for variance enthesis-to-fascia ratio, and 0.67 for composite index. GS: Grayscale; CON: Contrast; VAR: Variance; EFR: Enthsis-to-fascia ratio

## DISCUSSION

AS has both enthesal and axial skeletal structure changes, which, in turn, alter the function of spine and peripheral joints. Enthesitis is a main characteristic of AS and drives disease progression, which, in turn, causes spondylitis, synovitis, dactylitis, and enthesal bone damage.<sup>[12]</sup> In peripheral joints, normal entheses present fibrillar texture

on longitudinal B-mode US imaging, with a thin anechoic fibrocartilage seen between the tendon fibers and the bony cortex. For active enthesitis, the abnormal entheses display an increased thickness, a decreased echogenicity, and a loss of fibrillar pattern and often present Doppler signals. Notably, the enthesal area located within 2 mm above the bony cortex should be involved. Furthermore, chronic enthesopathy presents bony erosions, enthesophytes, and enthesal

**Table 3: Diagnostic values of gray-level co-occurrence matrix features of L4 supraspinous enthesis for ankylosing spondylitis**

	Cutoff value <sup>#</sup>	SEN (%)	SPE (%)	PPV (%)	NPV (%)
Inspection method	Abnormal echogenicity	19.1	86.4	75.0	33.3
Grayscale EFR	≥0.71	29.8	95.5	93.3	38.9
CON EFR	≥1.02	14.9	95.5	85.7	33.9
VAR EFR	≥0.71	25.5	95.5	91.7	36.8
Composite index*	≥2.06	31.9	95.5	93.3	38.9

\*Composite index=Grayscale EFR + CON EFR + VAR EFR, <sup>#</sup>Cutoff value was determined by the ROC curve (except for the inspection method).

SEN: Sensitivity, SPE: Specificity, PPV: Positive predictive value, NPV: Negative predictive value, EFR: Enthsis-to-fascia ratio, ROC: Receiver operating characteristic, CON: Contrast, VAR: Variance

**Table 4: The correlation between clinical features and echotexture features in ankylosing spondylitis patients**

	Disease duration	ESR	CRP	BASDAI	ASDAS-CRP
Grayscale EFR	-0.04	0.10	0.11	-0.22	-0.09
CON EFR	0.05	0.13	0.01	-0.25	-0.16
ENR EFR	-0.07	-0.10	-0.10	0.30	0.20
HOM EFR	-0.01	-0.02	-0.04	0.27	0.20
VAR EFR	-0.05	0.04	0.04	-0.25	-0.16

The Pearson's correlation coefficients (*r*) are shown in the table. ESR: Erythrocyte sedimentation rate, CRP: C-reactive protein, BASDAI: Bath ankylosing spondylitis disease activity index, ASDAS: Ankylosing spondylitis disease activity score, EFR: Enthsis-to-fascia ratio, CON: Contrast, ENR: Energy, HOM: Homogeneity, VAR: Variance

calcification.<sup>[13]</sup> The enthesis thickness and echogenicity are varied in chronic enthesopathy. Although peripheral joint enthesitis has been well studied, US changes of axial entheses, such as supraspinous entheses, have not yet been evaluated. It is also believed that B-mode US imaging may be a difficult method for evaluating axial entheses because there is no standard reference available.

Echotexture is a surface property that describes the patterns of structural arrangement of the surface on US images. Echotexture analysis is a quantitative method, which identifies the statistical properties. It contains first-order statistics, GLCM, and gray-level run length matrix. The mean GS value belongs to the first-order statistics features and is measured from the original image. The mean GS value does not consider the pixel neighbor relationship. Instead, GLCM considers the pixel neighbor relationship and extracts texture information from the original image to construct a co-occurrence matrix. There are several GLCM features with different mathematical definitions which are used to describe the characteristics of echotexture.<sup>[10]</sup> GLCM features had been used to aid in the diagnosis of both supraspinatus tendon tears and breast cancer seen on US images.<sup>[10,11]</sup> Here, we used echotexture analysis, including mean GS value and GLCM features, to identify the subtle changes in supraspinous enthesis. To overcome any errors in echogenicity caused by US machine settings and the skin thickness among different individuals, we adopted an EFR to eliminate these errors. The overlying thoracolumbar fascia is not affected by the disease, so it can be considered a standard.

The lumbar spine is typically involved earlier than the thoracic and cervical spines in the course of AS disease. Within the lumbar spine, the location of the L4 spinal process is more easily found by palpation than other lumbar spinal processes. This is

the reason why we chose the L4 spinal process for our study. Our results showed that L4 supraspinous enthesis in AS had a higher GS EFR, along with abnormal GLCM features, including a higher CON EFR, higher VAR EFR, and lower HOM EFR, in comparison to healthy controls. Conversely, while reading US images through use of the inspection method, both enthesis thickness and echogenicity in AS were not different from those in healthy controls. Thus, the obscure changes in supraspinous entheses in AS were undetectable by the inspection method, but could be identified by echotexture analysis. Our study has documented a new method using GLCM echotexture analysis for US assessment of supraspinous enthesopathy.

In chronic enthesopathy, interleukin (IL)-22 enhances mesenchymal stem cell osteogenesis and calcium production. These effects of IL-22 on mesenchymal stem cell function are a novel pathway for exploring pathological postinflammation osteogenesis in human spondyloarthropathies.<sup>[14]</sup> We presumed that chronic enthesopathy has more calcium components and would become brighter on a B-mode US image. This may explain why the GS value of L4 supraspinous enthesis was the higher in most of our AS patients.

There were some limitations in our study. First, the AS group had a wider range of GS EFR, CON EFR, and VAR EFR, which overlapped a great deal with those of the healthy group. This fact limited the diagnostic ability of echotextures and resulted in a relatively poor ROC curve (AUC, 0.64–0.70), so both the SEN and SPE could not be good. Second, we presumed that some entheses were in the subclinical inflammatory phase which would lower the GS value, the contract, and the VAR. Subsequently, this made for a wider range of these features among the AS group. However, these subclinically inflamed entheses could not be identified by either serum inflammatory

markers or clinical disease activity indices in our cohort. Third, GLCM features including GS EFR, CON EFR, and VAR EFR displayed a very low correlation with both CRP and ASDAS-CRP, so these features could not be indicators for AS disease activity.

## CONCLUSION

Echotexture analysis identified the subtle structural changes in L4 supraspinous enthesis in AS patients. It also showed significant differences in GS value and GLCM features between AS patients and healthy individuals. In addition, its analysis was superior to the inspection method and may have the potential to provide early detection of supraspinous enthesopathy in AS. Echotexture analysis may provide a role in AS diagnosis, while using the appropriate thresholds for GS value and GLCM features.

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## Conflicts of interest

There are no conflicts of interest.

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