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ORIGINAL ARTICLE

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Evaluation of disease chronicity by bone marrow fat fraction using sacroiliac joint magnetic resonance imaging in patients with spondyloarthritis: A retrospective study

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Abstract

Aim: This study investigated the use of fat fraction (FF) measurements in the sacroiliac (SI) joint to determine radiologic progression in patients with spondyloarthritis (SpA).

Method: A total of 138 patients who underwent pelvic magnetic resonance imaging (MRI) between September 2014 and March 2015 were retrospectively evaluated. The FF based upon fat deposition (%) using fat signaling on T1 and T2 weighted images in the sacroiliac joint was quantified using a 6-echo variant of the modified Dixon technique. We defined the normal bone marrow as normal FF, bone marrow edema as active inflammatory FF, and fat metaplasia as post-inflammatory FF.

Results: The mean FF of normal marrow was 52.0% ± 10.4% and 50.5% ± 10.1% in the left and right SI joints, respectively. The mean FF of post-inflammatory fat deposition was 81.9% ± 9.7% and 82.3% ± 9.6% in the left and right SI joints, respectively. The mean FF of active inflammatory fat deposition was 15.8% ± 5.9% and 13.5% ± 6.7% in the left and right SI joints, respectively. In multiple linear regression, post-inflammatory FF was found to be significantly associated with radiologic progression, such as symptom duration, SI joint grade, and modified Stoke Ankylosing Spondylitis Spine Score.

Conclusion: Post-inflammatory FF indicates the chronicity of SpA. Evaluating FF using MRI in the SI joint will help to determine radiologic progression.

KEYWORDS

fat fraction, magnetic resonance imaging, modified Dixon, sacroiliac joint, spondyloarthritis

1 | INTRODUCTION

Spondyloarthritis (SpA) is characterized by inflammation of the axial skeleton and peripheral joints.[1] The most characteristic feature of SpA is ankylosis and fusion of the axial joints, including the sacroiliac (SI) joint. The first imaging method used to diagnose sacroiliitis is plain radiography of the SI joints.[2] However, magnetic resonance imaging (MRI) is a useful alternative for select patients, such as young patients and those with a short symptom duration.[3]

Recent advances in rapid chemical-shift MRI have led to the development of imaging techniques, such as the modified Dixon (mDixon) method. This quantification method is able to measure fatty infiltration in various disease conditions, such as hepatic steatosis, intermuscular adipose tissue deposition, osteoporosis, and cancer. Additionally, the technique can be used in the diagnosis and evaluation of treatment response in these diseases.[4-6] In hematologic diseases, the assessment of bone marrow fat composition has been used as a marker of treatment response.[7,8]

Fat metaplasia is frequently observed in the bone marrow of the SI joints and spine in patients with SpA.[9,10] As the inflammation in the SI joint and spine recedes, fat metaplasia develops in its place. Previous attempts to assess fat change on MRI of the SI joint with standardized definitions and a semi-quantitative scoring method showed that fat metaplasia is a key intermediary step in the progression of ankyloses.[10] Several studies showed the usefulness of quantifying fat in bone marrow by measuring the fat fraction (FF) of patients with sacroiliitis in SpA.[11,12] However, those studies did not explain whether the quantification of fat in SI joints is related to radiologic progression or to the activity of SpA. The present study aimed to quantify bone marrow fat content in the SI joint of patients with SpA, using the mDixon Quant, and to evaluate its association with radiographic progression and disease activity.

2 | MATERIALS AND METHODS

2.1 | Clinical characteristics of patients

We retrospectively reviewed the records of 138 SpA patients who underwent MRI of the SI joints between September 2014 and March 2015. All patients were previously diagnosed with SpA according to the Assessment of Spondyloarthritis International Society classification criteria for axial SpA.[13] All patients gave informed consent in accordance with the Declaration of Helsinki. Hanyang University Seoul Hospital institutional review boards of all involved institutions approved this study (HYUH 2014-04-010).

Clinical characteristics including age, sex, symptom duration, human leukocyte antigen (HLA)-B27 positivity, history of uveitis, peripheral arthritis, and smoking were investigated. The serum erythrocyte sediment rate (ESR) and C-reactive protein (CRP) levels were obtained from electronic medical records. The Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and the Bath Ankylosing Spondylitis Functional Index (BASFI) were measured at the time of imaging study.[14,15] The radiographic progression was measured by characterizing the change in the SI joint on the basis of the New York criteria.[16] Spinal radiographs were scored using the modified Stoke Ankylosing Spondylitis Spine Score (mSASSS, 0-72).[17]

2.2 | Imaging protocol for FF

When the patients complained of inflammatory lower back pain, MRIs were taken to diagnose and differentiate between the causes of pain. MRIs were obtained on a 3.0-T imaging scanner (Ingenia; Philips Healthcare, Best, The Netherlands) with spine matrix coils. For FF signal quantification, data were acquired using a 3D proton density-weighted multi-gradient-echo sequence using receiver coil arrays with echo spacing of 1 ms The images were processed using the mDixon water/fat separation algorithm using a 6-echo variant.[18] The following six group images were obtained once the iterative decomposition of water and fat with echo asymmetry and least square estimation (IDEAL) sequence was scanned: in-phase image, out-of-phase image, pure water image, pure fat image, FF map, and R2* relaxation rate image. The FF measured are in fact the proton density FF (PDFF), as corrections for T2* effects and spectral complexity have been performed. The adipose contents of the fat infiltration regions (FIRs) were directly measured using the FF map, and the measurements represent the percentage of fat content in the local bone mass. This sequence automatically reconstructs FF images in the oblique coronal plane. The following parameters were used for FF images: repetition time = 8 ms, echo time = 1.2-1.37 ms, number of excitations = 3, echo train length = 6, field of view = 285-300 mm, matrix size = 190 × 190-200 × 200 pixels, section thickness = 4 mm, intersection gap = 2 mm, and flip angle = 3°.

2.3 | Quantification of bone marrow fat deposition

To classify FF images, we evaluated bone marrow fat deposition using Maksymowych et al's SI joint structural scoring system.[19] A normal bone marrow signal in the ilium and sacrum, which are far from the SI joint, was regarded as normal marrow fat (normal FF). When an area had high signal intensity on both T1- and T2-weighted images, it was regarded as a post-inflammatory fat deposition area (post-inflammatory FF). We used the same criterion to evaluate fat metaplasia, which means the lesion extended to more than 1 cm in depth from the joint space. When an area had low signal intensity on a T1-weighted image and high signal intensity on a fat-suppressed T2-weighted image, it was regarded as bone marrow edema and defined as an active inflammatory fat deposition (ie active inflammatory FF).

Almost all regions of interest (ROI) were chosen using anterior slices of the transitional slice, which means a visible portion of the cartilaginous portion of the joint. The FF was directly obtained by drawing a ROI approximately 30 mm^2 in size over the periarticular bone marrow on the automatically reconstructed FF image (Figure 1). The images were saved in a picture archiving and communication system (PACS; PiView STAR Version 5.0, Infinitt, Korea) at the maximum magnification. These ROIs were most often on the periarticular iliac side, which is a well-known SpA-affected site. The bone cortex and joint spaces were carefully avoided in all imaging sequences. If the entire cartilaginous portion of the SI joint was involved in post-inflammatory fat deposition or active inflammation, we drew an ROI for normal fat marrow at the ilial side of the ligamentous portion of the SI joint.

2.4 | Statistical analysis

All data were expressed as the means ± SD or percentage. The reliability of mSASSS and ROI for FF were assessed by two radiologists (S. Lee, Y. Song) and was independently evaluated with the intraclass correlation coefficient (ICC). Kernel density estimation with histogram was conducted to estimate the probability density function of normal, post-inflammatory, and active inflammatory FF. Simple and multiple linear regression analyses were conducted to examine the association between variables and the post-inflammatory FF. Logistic regression analysis with odds ratio (OR) was used to examine the influence of variables on the presence of active inflammation with bone marrow edema in the SI joint. Age, sex, and normal FF were adjusted using an adjusted model. P values <0.05

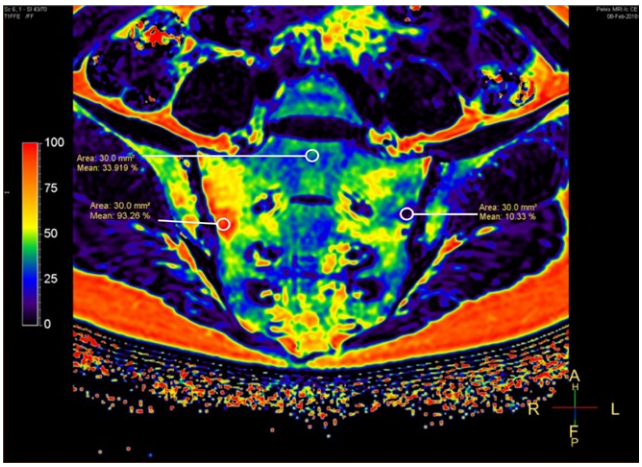

FIGURE 1 An example of color fat fraction (FF) (%) map from an oblique coronal image of the sacroiliac joint using the modified Dixon Quant. The post-inflammatory fat deposition regions (fat metaplasia) are red, normal marrow regions are green or yellow, and active inflammatory regions (edema) are blue. The changes in color according to FF (0%-100%) are represented by the bar graph on the right. An approximately 30 mm^2 region of interest (white circle) over the bone marrow was established to evaluate the FF

were assumed to indicate statistical significance. All statistical analyses were performed with R statistical language version 3.4.1.

3 | RESULTS

3.1 | Baseline clinical characteristics of patients

A total of 138 patients underwent MRI of the SI joints. Table 1 summarizes the baseline characteristics of patients. The mean patient age was 32.5 ± 11.8 years and mean symptom duration was 29.0 ± 6.0 months. Of these, nonsteroidal anti-inflammatory drugs (NSAIDs) were mostly used by 110 (79.7%) patients and 38 (27.5%) were taking disease-modifying anti-rheumatic drugs. Only eight patients (5.8%) were taking biologics. Serum ESR and CRP, which were evaluated at the time of performing MRI, were 23.0 ± 26.7 mm/h (0-15 mm/h) and 2.0 ± 6.3 mg/dL (0-0.8 mg/dL), respectively. The mean BASDAI and BASFI of patients were also elevated.

Two radiologists independently scored the radiographic changes. The inter-reader agreement regarding SI joint grade and the mSASSS was very good, with ICC of 0.997 (95% CI: 0.994-0.999) and 0.943 (95% CI: 0.941-0.995), respectively. The mean mSASSS score was 7.5 ± 7.6. The left and right SI joint grades were both 1.8 ± 1.3.

The normal and post-inflammatory FF agreement between the two measurements were also very good. The ICC of the left normal FF was 0.846 (95% CI: 0.783-0.890) and that for the right normal FF was 0.803 (95% CI: 0.723-0.860). The ICC of the left post-inflammatory FF was 0.909 (95% CI: 0.860-0.941) and that for the right post-inflammatory FF was 0.907 (95% CI: 0.855-0.941).

The mean FFs of the left and right joint normal FF were 52.0 ± 10.4 and 50.5 ± 10.1, respectively. The post-inflammatory FF was measured in 88 left SI joints and 84 right SI joints. The mean FFs of the left and right joint post-inflammatory FF were 81.9 ± 9.7 and 82.3 ± 9.6, respectively. Active inflammation with bone marrow edema was observed in 24 left SI joints and 29 right SI joints. The mean FFs of the left and right joint active inflammatory FF were 15.8 ± 5.9 and 13.5 ± 6.7, respectively.

TABLE 1 Baseline clinical characteristics of spondyloarthritis patients

	Value
Age, mean ± SD years	32.5 ± 11.8
Male, n (%)	92 (66.6)
Symptom duration, mean ± SD months	29.0 ± 6.0
HLA-B27 positivity, n (%)	92 (66.6)
History of uveitis, n (%)	12 (8.7)
History of peripheral arthritis, n (%)	13 (9.4)
History of smoking, n (%)	35 (25.3)
Current medication	
NSAIDs	110 (79.7)
DMARDs	38 (27.5)
Glucocorticoids	50 (36.2)
Biologics	8 (5.8)
ESR, mean ± SD mm/h	30.3 ± 34.2
CRP, mean ± SD mg/dL	2.4 ± 3.5
BASDAI, mean ± SD (n)	5.2 ± 2.4 (86)
BASFI, mean ± SD (n)	2.9 ± 3.0 (83)
SI joint grade, n (%)	Left/right
Grade 0	29 (21.0)/28 (20.3)
Grade I	27 (19.6)/31 (22.5)
Grade II	28 (20.3)/24 (17.4)
Grade III	46 (33.3)/48 (34.8)
Grade IV	8 (5.8)/7 (5.1)
mSASSS, mean ± SD (n)	7.5 ± 7.6 (72)
Fat fraction (mean ± SD)	Left/right
Normal fat marrow	52.0 ± 10.4/50.5 ± 10.1
Post-inflammatory fat fraction (n)	81.9 ± 9.7 (88)/82.3 ± 9.6 (84)
Active inflammatory fat fraction, left/right (n)	15.8 ± 5.9 (24)/13.5 ± 6.7 (29)

BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Spondylitis Functional Index; CRP, C-reactive protein; DMARDs, disease-modifying anti-rheumatic drugs; ESR, erythrocyte sedimentation rate; HLA, human leukocyte antigen; mSASSS, modified Stoke Ankylosing Spondylitis Spinal Score; NSAIDs, nonsteroidal anti-inflammatory drugs; SI, sacroiliac.

3.2 | Relationship between FF and radiographic change

The probability density with histograms of normal, post-inflammatory, and active inflammatory FF is described in Figure 2. Normal

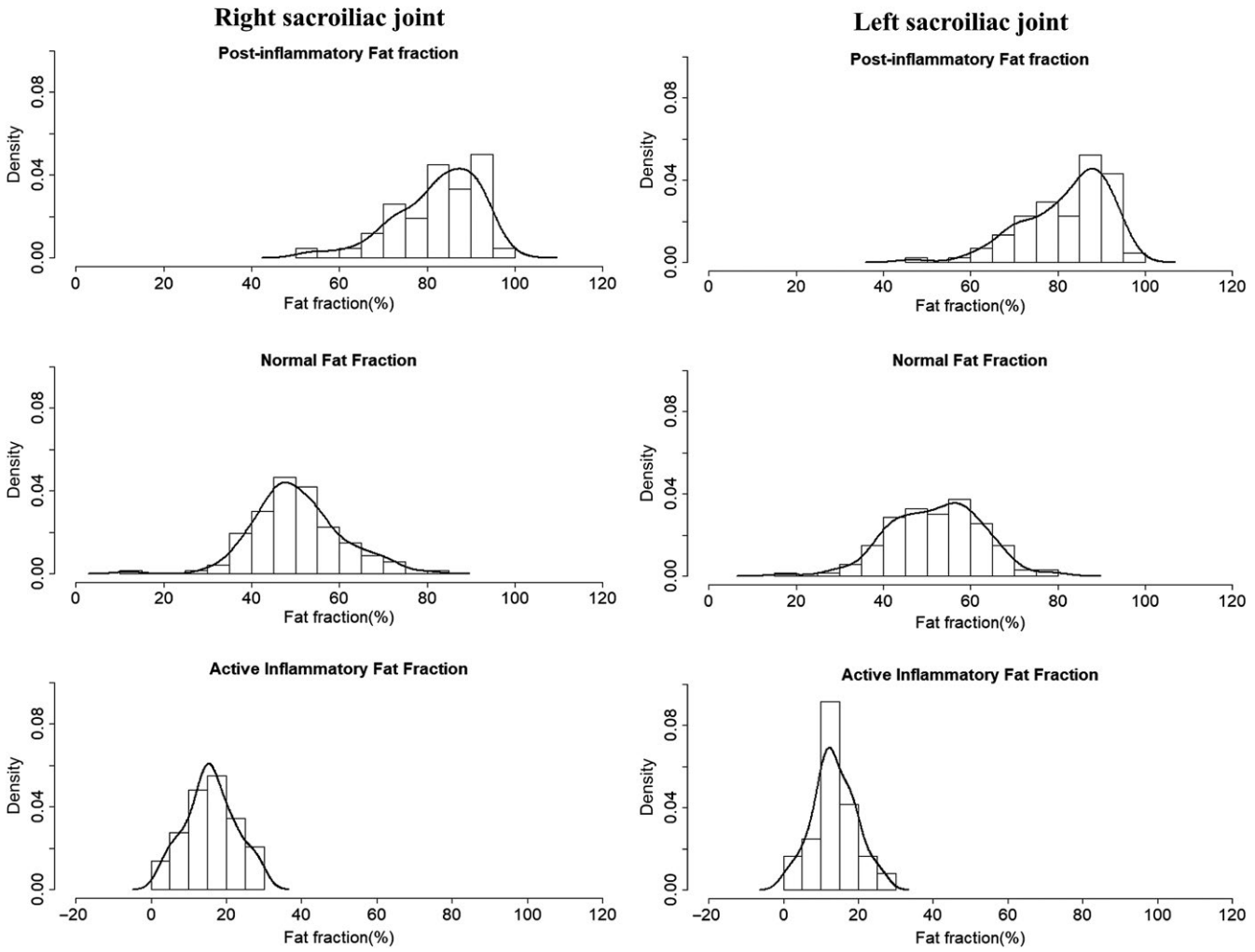

FIGURE 2 Distribution of fat fraction in the left and right sacroiliac joints. Kernel density estimation with histogram was used to construct a probability density curve

FF was mostly distributed between 30% and 80%. The proportion of fat deposition in the bone marrow was higher in post-inflammatory FF than normal FF and ranged from 60% to 100%. In the presence of active inflammation, the low FF was thought to be due to bone marrow edema and the range was approximately 0% to 30%. Figure 3 shows the variation of FF according to SI joint grade. Normal FF showed a generally constant FF value according to the grade change of the SI joint (Figure 3A,B). In contrast, post-inflammatory FF values appeared to increase slightly as the SI joint grade increased (Figure 3C,D). Post-inflammatory fat deposition was rarely observed in patients with a SI joint grade 0. Active inflammatory FF was mainly noted in grades 2 and 3 (Figure 3F). However, there appeared to be little difference in FF among grades.

Considering the possibility of the difference in FF due to symptom duration, patients were divided between groups with symptom duration of less than 3 months (Figure S1) and those with more than 3 months (Figure S2). However, the distribution of FF was similar to that noted in the whole patient group shown in Figure 3.

3.3 | Variables associated with post-inflammatory FF and active inflammatory FF

Table 2 shows the variables that were associated with post-inflammatory FF in linear regression analysis. Coefficients of symptom duration in the left and right were 0.49 ($P < 0.01$) and 0.32 ($P = 0.06$) in an unadjusted model and 0.58 ($P < 0.01$) and 0.42 ($P = 0.03$) in an adjusted model, respectively. Post-inflammatory FF was significantly associated with radiographic progression in the SI joint and spine. Coefficients of SI joint grade in the left and right were 5.05 ($P < 0.01$) and 3.78 ($P < 0.01$) in an unadjusted model and 4.57 ($P < 0.01$) and 3.44 ($P < 0.01$) in an adjusted model, respectively. Coefficients of mSASSS in the left and right were 0.41 ($P = 0.01$) and 0.37 ($P < 0.01$) in an unadjusted model and 0.37 ($P = 0.03$) and 0.37 ($P < 0.01$) in an adjusted model, respectively. However, variables related to disease activity, such as ESR, CRP, BASDAI, and active inflammatory FF were not associated with post-inflammatory FF.

Table 3 shows the variables that are associated with the presence of active inflammation in either of the SI joints. ESR was significantly associated with the presence of active inflammation (OR = 1.01,

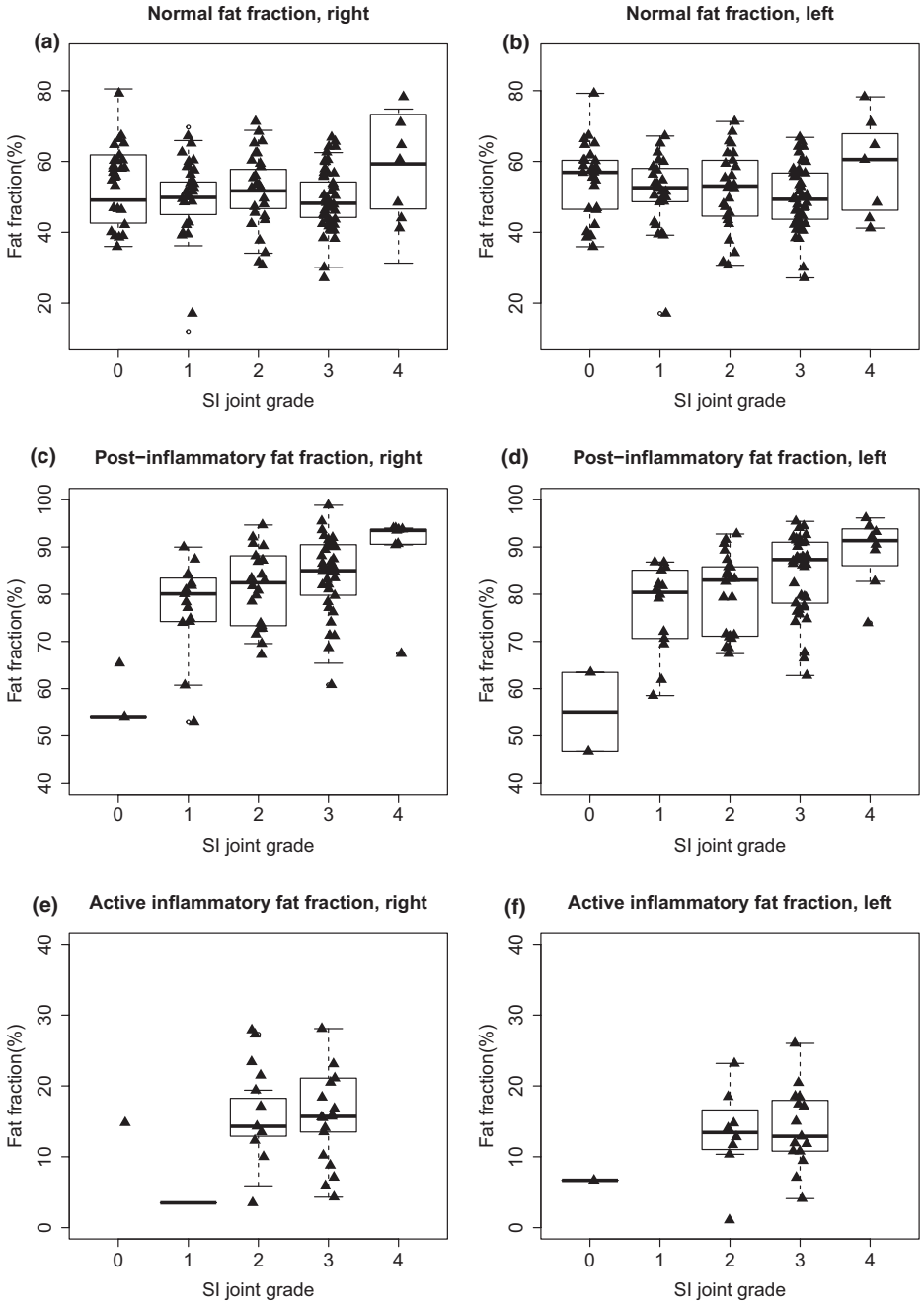

FIGURE 3 Box and scatter plots of normal (A and B), post-inflammatory (C and D), and active inflammatory (E and F) fat fractions according to the sacroiliac joint grade

$P = 0.05$ in the unadjusted model and OR = 1.02, $P < 0.01$ in the adjusted model). Symptom duration, CRP, BASDAI, and BASFI were not significantly associated with the presence of active inflammation. SI joint grade was significantly associated with the presence of active inflammation in the unadjusted (OR = 2.01, $P < 0.01$ in left and OR = 2.23, $P < 0.01$ in right) and adjusted (OR = 2.46, $P < 0.01$ in left and OR = 2.76, $P < 0.01$ in right) models, because many patients exhibited active inflammation at a high SI joint grade (Figure 2E,F). Post-inflammatory FF in patients with active inflammation showed a lower trend than in patients without active inflammation in unadjusted (OR = 0.95, $P = 0.03$ in left and OR = 0.97, $P < 0.17$ in right) and adjusted (OR = 0.95, $P < 0.05$ in left and OR = 0.97, $P < 0.25$ in right) models, although left post-inflammatory FF was significant.

4 | DISCUSSION

We evaluated radiologic progression in patients with SpA using the mDixon method according to the change in fat deposition in the SI joint, as indicated by MRI. Variables related with radiologic progression, such as symptom duration, SI joint grade, and mSASSS, were significantly associated with post-inflammatory FF in both SI

TABLE 2 Variables associated with post-inflammatory FF in the left and right sacroiliac joints

	Right sacroiliac joint				Left sacroiliac joint			
	Unadjusted model		Adjusted model[a]		Unadjusted model		Adjusted model[a]	
	Coefficient (95% CI)	*P* value	Coefficient (95% CI)	*P* value	Coefficient (95% CI)	*P* value	Coefficient (95% CI)	*P* value
Symptom duration	0.32 (−0.01 to 0.66)	0.06	0.42 (0.05-0.77)	0.03	0.49 (0.17-0.82)	<0.01	0.58 (0.23-0.93)	<0.01
ESR	−0.02 (−0.08 to 0.05)	0.64	−0.01 (−0.08 to 0.05)	0.69	−0.02 (−0.09 to 0.04)	0.42	−0.02 (−0.08 to 0.04)	0.47
CRP	−0.18 (−0.69 to 0.32)	0.47	−0.04 (−0.53 to 0.44)	0.86	−0.19 (−0.68 to 0.31)	0.46	−0.06 (−0.56 to 0.43)	0.80
BASDAI	−1.25 (−2.23 to −0.26)	0.01	−0.76 (−1.81 to 0.29)	0.15	−0.87 (−1.89 to 0.16)	0.09	−0.23 (−1.41 to 0.95)	0.70
BASFI	−0.27 (−1.34 to 0.79)	0.61	−0.06 (−1.12 to 1.00)	0.91	−0.31 (−1.41 to 0.78)	0.57	−0.02 (−1.13 to 1.09)	0.97
SI joint grade	3.78 (1.73-5.84)	<0.01	3.44 (1.47-5.41)	<0.01	5.05 (3.13-6.97)	<0.01	4.57 (2.66-6.48)	<0.01
mSASSS	0.42 (0.13-0.71)	<0.01	0.37 (0.10-0.65)	<0.01	0.41 (0.08-0.73)	0.01	0.37 (0.05-0.68)	0.03
Active inflammatory FF	−0.14 (−0.85 to 0.57)	0.68	−0.04 (−0.72 to 0.65)	0.91	−0.39 (−1.26 to 0.49)	0.36	−0.53 (−1.07 to 0.63)	0.34

BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Spondylitis Functional Index; CI, confidence interval; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; FF, fat fraction; mSASSS, modified Stoke Ankylosing Spondylitis Spinal Score; SI, joint sacroiliac.

[a]Adjusted for age, sex, and normal FF.

joints. The proportion of fat deposition was higher as the disease progressed, which was higher than in the normal bone marrow. Meanwhile, in cases of active inflammation, FF was low and there was bone marrow edema.

Fat quantification has been used for the diagnosis and treatment of various diseases.[7,8] FF of the spine is an established parameter in osteoporotic patients. Ergen et al studied FF and bone mineral density (BMD) in 45 consecutive women[20] and discovered a negative correlation between BMD and FF. The mean FFs of healthy patients and those with osteopenia and osteoporosis were 45.17% ± 1.3%, 51.77% ± 0.69%, and 50.82% ± 1.5%, respectively. In other studies using different techniques to measure fat content, the mean FF of the spine was approximately 45%-56% and 57%-65% in healthy and osteoporotic patients, respectively.[21-23]

There were two studies that investigated fat quantification of SI joint in SpA.[11,12] Bray et al measured bone marrow composition in terms of PDFF using chemical shift-encoded MRI in patients with SpA.[11] They showed that PDFF measurements accurately reflect changes in the bone marrow composition in normal bone marrow, bone marrow edema, and fat metaplasia. They also showed that R2* measurements are reduced in areas of fat metaplasia due to a reduction in BMD. Guo et al measured and compared fat deposition in fat-infiltrated regions and normal-appearing regions of patients with ankylosing spondylitis with iterative decomposition of water and fat with echo asymmetry and least square estimation (IDEAL).[12] They identified that the fat infiltration regions and normal-appearing regions were reduced in those who underwent active treatment for 6 months. These two studies applied fat quantification of SI joints using a method similar to our mDixon method. However, our study investigated not only the measurement of FF in bone marrow lesions, but also its association with other clinical factors in a relatively large number of patients.

The FF of the post-inflammatory fat deposition region was higher than that of normal bone marrow and healthy controls, and even in osteoporotic FF in the fat fraction studies of bone marrow. It was an important finding that the post-inflammatory FF measured at the ROI of the most severe region of fat metaplasia correlated with the progression of SpA, which was not done in the two studies that measured the FF of the SI joints.[11,12] This showed that the measurement of FF can be another method for indicating the progression of SpA. In addition, we suggested that FF of the spine can also indicate the progression of SpA based on the relationship between mSASSS and post inflammatory FF in the SI joints in our results.

In terms of acute inflammation of the SI joints, we determined that the acute inflammatory FF in the bone marrow had a lower fat signal than the normal marrow region. The presence of active inflammation was associated with increased ESR and was mostly found in patients with SI joint grades 2 and 3. Although CRP may reflect disease activity,[24] CRP was not associated with active inflammatory FF in our study. This is because the number of patients with active inflammatory FF was too small, and some patients with active inflammatory FF had normal CRP values (<0.8 mg/dL). Interestingly, patients who had active inflammation showed

TABLE 3 Variables associated with the presence of active inflammation in the sacroiliac joint

	Unadjusted model		Adjusted model[a]	
	Odds ratio (95% CI)	*P* value	Odds ratio (95% CI)	*P* value
Symptom duration	0.39 (0.88-1.03)	0.29	0.99 (0.90-1.08)	0.87
ESR	1.01 (1.00-1.02)	0.05	1.02 (1.01-1.03)	<0.01
CRP	1.03 (0.92-1.13)	0.63	1.04 (0.92-1.17)	0.47
BASDAI	0.99 (0.81-1.20)	0.89	0.99 (0.78-1.24)	0.91
BASFI	0.98 (0.82-1.14)	0.80	0.94 (0.76-1.11)	0.49
SI joint grade, left	2.01 (1.41-3.00)	<0.01	2.46 (1.61-4.05)	<0.01
SI joint grade, right	2.23 (1.54-3.41)	<0.01	2.76 (1.77-4.47)	<0.01
mSASSS	0.96 (0.87-1.03)	0.36	0.96 (0.86-1.04)	0.43
Post-inflammatory FF, left	0.95 (0.90-0.99)	0.03	0.95 (0.90-1.00)	0.05
Post-inflammatory FF, right	0.97 (0.92-1.01)	0.17	0.97 (0.91-1.02)	0.25

BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Spondylitis Functional Index; CI, confidence interval; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; FF, fat fraction; mSASSS, modified Stoke Ankylosing Spondylitis Spinal Score; SI, joint sacroiliac.

[a]Adjusted for age, sex, and normal FF.

decreased post-inflammatory FF compared to patients without active inflammation. This may be attributable to a lower FF with the overlapping of active inflammation in post-inflammatory fat deposition.

Osteoblasts and adipocytes from marrow mesenchymal stem cells are precursors of bone remodeling.[25] Our study demonstrated a large accumulation of fat in the bone marrow of the subchondral region of the SI joint. This finding might represent a different mechanism than that seen in osteoporotic changes of the bone marrow. Appel et al showed inflammation and fibrotic change in the subchondral bone marrow in the facet joints of patients with AS.[26] In addition, they also found that interleukin-23-positive inflammatory cells were involved in the bone changes in chronic AS. The inflammatory changes in SpA differ from those in osteoporosis, and this inflammation might influence fat metaplasia of the subchondral bone in SpA.[10]

Our study has several limitations. First, although there was a good correlation between observers in terms of FF, the FF values may differ because the ROI between the observers can differ. However, since the ROI was determined by analyzing the T1 and T2 images, the error between the measurements was small. Further research will be needed to standardize the FF measurement method with either overall measurement of the SI joint or through automated measurements. Second, we did not correct for bone-related diseases such as osteoporosis. In our study, although the adjusted FF for age and sex were obtained, the results may vary slightly depending on the presence or absence of osteoporosis. Third, although we selected the ROI to measure the FF using T1- and T2-weighted images, it may be intrinsically subjective.

We measured the FF in the SI joints of SpA patients and presented a range of normal, post-inflammatory, and active inflammatory FFs according to the proportion of fat deposition. We found that the fat deposition in SI joints increases with the progression of SpA. FF maps using the mDixon technique were not only helpful in evaluating the chronicity of SpA, but also may be a useful tool in studying its pathogenesis in such patients.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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REFERENCES

1. Khan MA, van der Linden SM. A wider spectrum of spondyloarthropathies. *Semin Arthritis Rheum*. 1990;20:107-113.
2. van der Heijde D, Landewe R. Imaging in spondylitis. *Curr Opin Rheumatol*. 2005;17:413-417.
3. Mandl P, Navarro-Compan V, Terslev L, et al. EULAR recommendations for the use of imaging in the diagnosis and management of spondyloarthritis in clinical practice. *Ann Rheum Dis*. 2015;74:1327-1339.
4. Kim H, Taksali SE, Dufour S, et al. Comparative MR study of hepatic fat quantification using single-voxel proton spectroscopy, two-point dixon and three-point IDEAL. *Magn Reson Med*. 2008;59:521-527.
5. Alizai H, Nardo L, Karampinos DC, et al. Comparison of clinical semi-quantitative assessment of muscle fat infiltration with quantitative assessment using chemical shift-based water/fat separation in MR studies of the calf of post-menopausal women. *Eur Radiol*. 2012;22:1592-1600.
6. Li GW, Xu Z, Chen QW, et al. Quantitative evaluation of vertebral marrow adipose tissue in postmenopausal female using

MRI chemical shift-based water-fat separation. *Clin Radiol*. 2014;69:254-262.
7. Li J, Law HK, Lau YL, Chan GC. Differential damage and recovery of human mesenchymal stem cells after exposure to chemotherapeutic agents. *Br J Haematol*. 2004;127:326-334.
8. Oriol A, Valverde D, Capellades J, Cabanas ME, Ribera JM, Arus C. In vivo quantification of response to treatment in patients with multiple myeloma by 1H magnetic resonance spectroscopy of bone marrow. *MAGMA*. 2007;20:93-101.
9. Chiowchanwisawakit P, Lambert RG, Conner-Spady B, Maksymowych WP. Focal fat lesions at vertebral corners on magnetic resonance imaging predict the development of new syndesmophytes in ankylosing spondylitis. *Arthritis Rheum*. 2011;63:2215-2225.
10. Maksymowych WP, Wichuk S, Chiowchanwisawakit P, Lambert RG, Pedersen SJ. Fat metaplasia and backfill are key intermediaries in the development of sacroiliac joint ankylosis in patients with ankylosing spondylitis. *Arthritis Rheumatol*. 2014;66:2958-2967.
11. Bray T, Bainbridge A, Punwani S, Ioannou Y, Hall-Craggs MA. Simultaneous quantification of bone edema/adiposity and structure in inflamed bone using chemical shift-encoded MRI in spondyloarthritis. *Magn Reson Med*. 2018;79:1031-1042.
12. Guo RM, Lin WS, Liu WM, et al. Quantification of fat infiltration in the sacroiliac joints with ankylosing spondylitis using IDEAL sequence. *Clin Radiol*. 2018;73:231-236.
13. Rudwaleit M, van der Heijde D, Landewe R, 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;68:777-783.
14. Calin A, Garrett S, Whitelock H, et al. A new approach to defining functional ability in ankylosing spondylitis: the development of the Bath Ankylosing Spondylitis Functional Index. *J Rheumatol*. 1994;21:2281-2285.
15. Garrett S, Jenkinson T, Kennedy LG, Whitelock H, Gaisford P, Calin A. A new approach to defining disease status in ankylosing spondylitis: the Bath Ankylosing Spondylitis Disease Activity Index. *J Rheumatol*. 1994;21:2286-2291.
16. van der Linden S, Valkenburg HA, Cats A. Evaluation of diagnostic criteria for ankylosing spondylitis. A proposal for modification of the New York criteria. *Arthritis Rheum*. 1984;27:361-368.
17. Creemers MC, Franssen MJ, van't Hof MA, Gribnau FW, van de Putte LB, van Riel PL. Assessment of outcome in ankylosing spondylitis: an extended radiographic scoring system. *Ann Rheum Dis*. 2005;64:127-129.
18. Kukuk GM, Hittatiya K, Sprinkart AM, et al. Comparison between modified Dixon MRI techniques, MR spectroscopic relaxometry, and different histologic quantification methods in the assessment of hepatic steatosis. *Eur Radiol*. 2015;25:2869-2879.
19. Maksymowych WP, Pitts M, Budak MJ, et al. Development and preliminary validation of a digital overlay-based learning module for semiquantitative evaluation of magnetic resonance imaging lesions in osteoarthritis of the hip. *J Rheumatol*. 2015;43:232-238.
20. Ergen FB, Gulal G, Yildiz AE, Celik A, Karakaya J, Aydingoz U. Fat fraction estimation of the vertebrae in females using the T2*-IDEAL technique in detection of reduced bone mineralization level: comparison with bone mineral densitometry. *J Comput Assist Tomogr*. 2014;38:320-324.
21. Schellinger D, Lin CS, Lim J, Hatipoglu HG, Pezzullo JC, Singer AJ. Bone marrow fat and bone mineral density on proton MR spectroscopy and dual-energy X-ray absorptiometry: their ratio as a new indicator of bone weakening. *AJR Am J Roentgenol*. 2004;183:1761-1765.
22. Wehrli FW, Hopkins JA, Hwang SN, Song HK, Snyder PJ, Haddad JG. Cross-sectional study of osteopenia with quantitative MR imaging and bone densitometry. *Radiology*. 2000;217:527-538.
23. Yeung DK, Griffith JF, Antonio GE, Lee FK, Woo J, Leung PC. Osteoporosis is associated with increased marrow fat content and decreased marrow fat unsaturation: a proton MR spectroscopy study. *J Magn Reson Imaging*. 2005;22:279-285.
24. Lorenzin M, Ortolan A, Vio S, et al. Biomarkers, imaging and disease activity indices in patients with early axial spondyloarthritis: the Italian arm of the SpondyloArthritis-Caught-Early (SPACE) Study. *Reumatismo*. 2017;69:65-74.
25. Justesen J, Stenderup K, Ebbesen EN, Mosekilde L, Steiniche T, Kassem M. Adipocyte tissue volume in bone marrow is increased with aging and in patients with osteoporosis. *Biogerontology*. 2001;2:165-171.
26. Appel H, Maier R, Bleil J, et al. In situ analysis of interleukin-23- and interleukin-12-positive cells in the spine of patients with ankylosing spondylitis. *Arthritis Rheum*. 2013;65:1522-1529.

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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