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ORIGINAL RESEARCH

Utility of Magnetic Resonance Imaging in Assessing Disease Activity in Axial Spondyloarthritis Regardless of C-Reactive Protein Status

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Background: Magnetic resonance imaging (MRI) and C-reactive protein (CRP) are commonly utilized in the diagnostic and disease activity assessment of axial spondyloarthritis (axSpA). The aim of this analysis is to determine the clinical utility of MRI and CRP in assessing disease activity, particularly in patients with normal CRP levels.

Methods: A retrospective evaluation was conducted on patients diagnosed with axSpA who received care at the First Affiliated Hospital of Fujian Medical University between 2022 and 2024. Comparisons were made between patients diagnosed with ankylosing spondylitis (AS) and those with non-radiographic axial spondyloarthritis (nr-axSpA) regarding clinical features, disease activity, and MRI-detected lesions.

Results: A total of 719 patients diagnosed with axSpA were included. Of the 638 patients who underwent both MRI and CRP testing, 391 had normal CRP levels, and 247 had elevated CRP levels. Among patients with normal CRP levels, the frequency of active and structural lesions identified on MRI was significantly lower compared to those with elevated CRP levels ($p < 0.05$). Within the nr-axSpA group, the detection rate of erosive, active and structural combined lesions was significantly lower in patients with normal CRP levels compared to those with elevated CRP levels. When compared with MRI, the sensitivity and specificity of CRP in detecting active and structural lesions remained below 80%.

Conclusion: In patients with normal CRP levels, MRI remains a valuable tool for evaluating disease activity in axSpA. The imaging findings indirectly indicate that erosive changes may represent an early stage in the progression from bone marrow edema to structural damage. Nr-axSpA may reflect an earlier disease stage, whereas AS represents a later stage within the axSpA spectrum.

Keywords: ankylosing spondylitis, axial spondyloarthritis, magnetic resonance imaging, non-radiographic axial spondyloarthritis, spondyloarthritis, CRP, disease activity

Introduction

Axial spondyloarthritis (axSpA) refers to a group of heterogeneous inflammatory rheumatic disorders that predominantly involve the axial skeleton, peripheral joints, and entheses. Common clinical manifestations include inflammatory back pain, dactylitis, enthesitis, and ligamentous ossification, all of which contribute to substantial impairments in physical functioning and quality of life among patients. AxSpA encompasses both radiographic axial spondyloarthritis, also referred to as ankylosing spondylitis (AS), and non-radiographic axial spondyloarthritis (nr-axSpA).[1,2]

Assessment of disease activity in axSpA typically involves composite indices such as the Ankylosing Spondylitis Disease Activity Score with C-reactive protein (ASDAS-CRP), Bath Ankylosing Spondylitis Disease Activity Index

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(BASDAI), Bath Ankylosing Spondylitis Metrology Index (BASMI), and Bath Ankylosing Spondylitis Functional Index (BASFI), in addition to biomarkers such as C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR). However, in high-demand clinical settings, the use of comprehensive scoring systems may be impractical. CRP and ESR, as widely adopted markers of systemic inflammation, are typically elevated during active inflammatory states.[3] The traditional clinical assessment tools do not include imaging modalities such as MRI. Consequently, patients may exhibit normal scores on conventional disease activity measures (eg, CRP or ASDAS-CRP) while still experiencing ongoing radiographic progression. In such cases, dose reduction or discontinuation may lead to disease flare or even structural progression to ankylosis.

Previous findings have indicated that individuals with normal magnetic resonance imaging (MRI) and CRP levels at baseline may subsequently develop clinical symptoms and exhibit objective evidence of inflammation.[4] CRP is commonly utilized for the clinical evaluation of disease activity, with elevated levels in axSpA being considered one of the most reliable indicators of both treatment response and radiographic progression.[5] Despite this, clinical follow-up has revealed that some patients with active axSpA may present with normal CRP levels.

Historically, clinical attention has focused primarily on active lesions visible on MRI, such as bone marrow edema (BME), capsulitis, and enthesitis, and the role of MRI in early diagnosis. Preliminary evidence supports MRI's high sensitivity and specificity in detecting both active and structural lesions within the spine and sacroiliac joints (SIJ). Recent literature further supports MRI's role in monitoring disease activity and prognosis during treatment of axSpA.[6] In light of this, the aim of the present study is to evaluate the clinical utility of CRP and MRI in assessing disease activity in routine practice. In addition, the objective of this study was to examine the clinical characteristics and MRI diagnostic value in patients with axSpA and normal levels of serum inflammatory markers. To facilitate the evaluation of treatment response and guide subsequent therapeutic decisions in axSpA patients with normal CRP and subjective well-being, MRI examination is recommended to prevent disease progression to ankylosis and subsequent significant impairment of quality of life.

Materials and Methods

Study Design and Participants

A retrospective analysis was conducted on patients who underwent 3.0T-MRI scans at the First Affiliated Hospital of Fujian Medical University from August 2022 to August 2024 and met the ASAS axSpA classification criteria or the modified New York (mNY) criteria.[7,8] All participants were aged over 18 years. Patients were categorized into normal CRP and abnormal CRP groups based on diagnostic criteria. Two rheumatologists independently recorded clinical symptoms, medical histories, physical examination findings, laboratory test results, sacroiliac joint X-rays, and 3.0T-MRI outcomes.

Due to the higher false-positive rates associated with MRI in athletes and pregnant women, women with pregnancy-related low back pain or those participating in high-intensity sports, such athletes, were excluded.[9–11] Other exclusion criteria included autoimmune diseases unrelated to axSpA, chronic infections, tumors, severe organ failure, and mental health disorders.

Ethical approval for this study was granted by the Research Ethics Committee of the First Affiliated Hospital of Fujian Medical University (reference number: MRCTA, FMU ECFAH[2018]198). In accordance with the Helsinki Declaration V, written informed consent was obtained from all participants prior to their inclusion in the study.

Clinical Assessment

General information collected from participants included age, gender, disease duration, inflammatory back pain, family history of axSpA, and the presence of any extra-articular manifestations (including psoriasis, inflammatory bowel disease, and uveitis). Outcome measures for axSpA, based on the report by Zochling et al, were recorded and included ASDAS-CRP, BASDAI, BASFI, and BASMI.[12] Additional data regarding past and current anti-rheumatic treatments, such as nonsteroidal anti-inflammatory drugs (NSAIDs), conventional synthetic Disease-Modifying Anti-rheumatic

Drugs (csDMARDs), and biologic DMARDs (bDMARDs), were documented. Peripheral arthritis was defined as the presence of pain, swelling, and/or tenderness in any peripheral joint, excluding the shoulder and hip joints.

Laboratory Assessment

Laboratory assessments included the determination of Human Leukocyte Antigen B27 (HLA-B27; flow cytometry method, Beckman Coulter, Inc)., CRP (mg/L; immunoturbidimetric method, Beckman Coulter, Inc)., and ESR (mm/h). CRP and MRI were tested concurrently, with no more than one week between measurements. There were no restrictions on whether MRI completion or CRP testing occurred during initial or subsequent treatment for axSpA. CRP normal means CRP is less than 6.0 mg/L, meanwhile CRP abnormal means CRP is more than 6.0 mg/L.

MRI Scoring

MRI scans were evaluated by two independent assessors: one was an experienced radiologist with expertise in interpreting axSpA MRI scans, and the other was a rheumatologist trained in MRI analysis.

The 3.0T-MRI scans of the sacroiliac joints were analyzed using the SPARCC (Spondyloarthritis Research Consortium of Canada) scoring system. Primary lesions of the sacroiliac joints included BME, erosions, backfill, fat metaplasia, and ankylosis. The frequency of these imaging findings was recorded. MRI sequences used included T1-weighted imaging (T1 WI-TRA/COR), T2-weighted imaging (T2 WIFS-COR/TRA), and VIBE/e-THRIVE.

An MRI of the sacroiliac joints was considered positive for active sacroiliitis when BME was clearly visible in typical anatomical regions (subchondral bone) on T2-weighted sequences, spanning at least two consecutive slices of the MRI.[13] Fat metaplasia was characterized as a bright signal on T1-weighted non-fat-suppressed sequences, brighter than normal bone marrow, and meeting specific criteria: (a) uniform brightness, (b) located in typical anatomical regions (subchondral bone), and (c) clearly demarcated from normal bone marrow along its non-articular borders.[13] Erosions were defined as bone defects at the joint margins, involving the entire cartilage compartment of the joint, and could present as single lesions or confluent erosions/pseudowidening.[14] Fat metaplasia within erosion cavities, referred to as "backfill", is considered an intermediate stage between erosion and ankylosis and appears as an imaging sign in the cartilage portion of the sacroiliac joint when extensive iliac erosions are present. Backfill is characterized by fat-equivalent signal intensity, irregular sclerotic margins, and orientation toward unerosive bone.[15] Ankylosis was identified as an abnormally bright signal on T1-weighted non-fat-suppressed sequences, with signal intensity similar to bone marrow, located in the expected position of the sacroiliac joint space, bridging the joint and creating a continuous signal between the ilium and sacrum.[16] The absence of the dark appearance of the subchondral cortical bone on both sides of the joint was also noted.[13] Osteophytes were recognized as abnormally bright signals on T1-weighted non-fat-suppressed sequences, with signal intensity similar to that of bone marrow, located at the expected position of the sacroiliac joint space, bridging the joint, and continuous with the subchondral bone of either the ilium or sacrum, but not both.[13]

Consequently, the standard SPARCC scoring on 6/5 semi-coronal MRI slices was utilized to assess inflammation and structural lesions in patients with axSpA. Detection of inflammation on a single slice required evidence of multiple inflammatory lesions.[17]

Data Analysis

Statistical analysis was performed using MedCalc software. Intergroup differences were assessed using *t*-tests, chi-squared (χ^2) tests, or Fisher's exact probability method. A value of $p < 0.05$ was considered statistically significant. Missing data were addressed using multiple imputation methods. Since axSpA can be classified into AS and nr-axSpA based on radiographic findings, the authors divided axSpA into these two groups for post-hoc analysis.

Results

Between 2022 and 2024, a total of 719 individuals were screened, among whom 638 met the inclusion criteria and completed both MRI and CRP assessments. The axSpA cohort was initially stratified into normal and abnormal CRP groups. A subsequent post hoc analysis further categorized the cohort into AS and nr-axSpA groups, each also divided according to CRP levels (Figure 1).

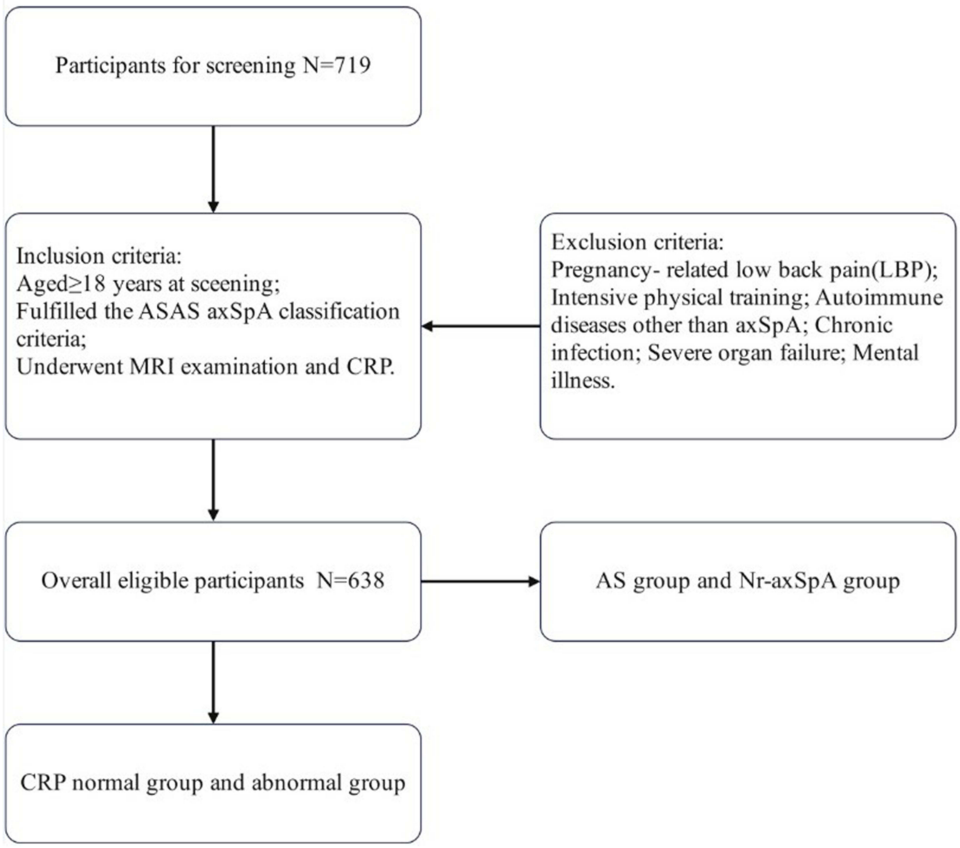

Figure 1 Flowchart of participants selection.

Overall, 60.82% of participants were male, with a median age of 36 years. The median symptom duration at the first visit was 71.62 months, and 37.15% of patients were classified with nr-axSpA. Low back pain (LBP) was reported by 28.37%, while 33.39% presented with peripheral arthritis. The majority were HLA-B27 positive. More than half of the patients (65.83%, n = 420) were receiving treatment with NSAIDs, 22.73% (n = 145) were receiving csDMARDs, and 26.18% (n = 167) were receiving bDMARDs. The ASDAS-CRP scores ranged from 0 to 4, with a mean value of 2.60. BASDAI scores ranged from 0 to 10, with a mean of 3.40. Compared to the abnormal CRP group (n = 247), the normal CRP group (n = 391) included a lower proportion of male patients, a higher rate of nr-axSpA, a lower prevalence of LBP history, and a reduced HLA-B27 positivity rate ($p < 0.05$; Table 1).

The detection rates of BME, erosion, fat metaplasia, backfill, and ankylosis in patients with axSpA were 57.05% (n = 364), 53.45% (n = 341), 18.65% (n = 119), 16.77% (n = 107), and 14.73% (n = 94), respectively. The incidence of BME, erosion, fat metaplasia, backfill, ankylosis, and combined active and structural lesions was significantly lower in the normal CRP group than in the abnormal CRP group (Table 2).

In a post hoc analysis, patients were stratified into AS and nr-axSpA groups. The mean baseline CRP level was 11.56 mg/L. Compared to the nr-axSpA group, the AS group had a higher proportion of male patients (66.75%, n = 269), a greater frequency of peripheral arthritis (26.55%, n = 107), a longer duration of symptoms (84.66 months), higher prevalence of LBP history (87.59%, n = 353), and a higher HLA-B27 positivity rate (87.10%), all with statistically significant differences ($p < 0.05$). Additionally, a higher proportion of patients in the AS group received bDMARDs therapy (32.01%, n = 129; Table 3).

Among patients with AS, the detection rates of BME (60.55%, n = 244), erosion (67.74%, n = 273), fat metaplasia (25.81%, n = 104), backfill (24.07%, n = 97), ankylosis (23.33%, n = 94), and combined active and structural lesions were higher than in patients with nr-axSpA, with statistically significant differences (Appendix Table 1).

Table 1 Clinical Characteristics of axSpA Patients with CRP Normal and CRP Abnormal [$x \pm s$ or n(%)]

Variables	Total (n=638)	CRP Normal (n=391)	CRP Abnormal (n=247)	*P* value
Male, n (%)	388(60.82)	201(51.41)	187(75.71)	<0.001
Age at enrollment (years)	36.03±12.90	35.79±13.04	36.41±12.69	0.645
Symptom duration at first visit (months)	71.62±82.19	72.68±79.78	69.95±86.00	0.188
Nr-axSpA, n (%)	237(37.15)	170(43.48)	67(27.13)	<0.001
History of LBP, n (%)	181(28.37)	129(32.99)	52(21.05)	0.001
Peripheral arthritis, n (%)	213(33.39)	127(32.48)	86(34.82)	0.524
Family history of SpA, n (%)	62(9.72)	41(10.49)	21(8.50)	0.41
History of IBD, n (%)	11(1.72)	7(1.79)	4(1.62)	0.872
History of psoriasis, n (%)	21(3.29)	10(2.56)	11(4.45)	0.191
HLA-B27, n (%)	521(81.66)	302(77.24)	219(88.66)	<0.001
Drug used information, n (%)				
bDMARDs	167(26.18)	120(30.69)	47(19.03)	0.001
NSAIDs	420(65.83)	264(67.52)	156(63.16)	0.258
csDMARDs	145(22.73)	90(23.02)	55(22.27)	0.826
ASDAS-CRP	2.60±1.21	1.91±1.10	3.39±1.00	0.622
BASDAI	3.40±1.99	3.16±1.96	4.00±1.85	0.765
BASFI	1.99±2.64	1.29±1.91	2.93±3.16	0.01
BASMI	2.11±2.44	1.44±2.26	3.00±2.54	0.538

Notes: Male, Nr-axSpA, History of LBP, Peripheral arthritis, Family history of SpA, History of IBD, History of psoriasis, HLA-B27, Drug used information used $\chi 2$ test. Age at enrollment, Symptom duration at first visit, ASDAS-CRP, BASDAI, BASFI, BASMI used *t*-test.

Table 2 The MRI Lesions of axSpA Patients with CRP Normal and CRP Abnormal [n(%)]

Variables	Total (n=638)	Normal CRP (n=391)	CRP Abnormal (n=247)	*P* value
BME	364(57.05)	209(53.45)	155(62.75)	0.021
Erosion	341(53.45)	196(50.13)	145(58.70)	0.035
Fat metaplasia	119(18.65)	63(16.11)	56(22.67)	0.038
Backfill	107(16.77)	51(13.04)	56(22.67)	0.002
Ankylosis	94(14.73)	34(8.70)	60(24.29)	<0.001
BME+ Erosion	240(37.62)	123(31.46)	117(47.37)	<0.001
BME+ Fat metaplasia	66(10.34)	32(8.18)	34(13.77)	0.024
BME+ Backfill	79(12.38)	36(9.21)	43(17.41)	0.002

Notes: Tested by $\chi 2$ tes t.
Abbreviation: BME, bone marrow edema.

No cases of ankylosis were identified in the nr-axSpA group. Both AS and nr-axSpA groups were further stratified by CRP levels. In the AS group, the detection rates of BME, erosion, fat metaplasia, backfill, and combined active and structural lesions were similar between the normal and abnormal CRP subgroups (Appendix Table 1). However, in the nr-axSpA group, the detection rates of erosion and combined active and structural lesions were significantly lower in the normal CRP subgroup than in the abnormal CRP subgroup (Appendix Table 1).

This study evaluated the utility of CRP in assessing disease activity in AS and nr-axSpA, using MRI-detected active and structural lesions as the reference standard. Among patients with axSpA, CRP sensitivity and specificity ranged from

Table 3 Clinical Characteristics of Patients with AS and Nr-axSpA [x ± s or n(%)]

Variables	Total (n=638)	AS (n=403)	nr-axSpA (n=235)	*P* value
Male, n (%)	388(60.82)	269(66.75)	119(50.64)	<0.001
Age at enrollment (years)	36.03±12.90	36.17±12.57	35.79±13.48	0.222
Symptom duration at first visit (months)	71.62±82.19	84.66±89.32	49.32±62.44	<0.001
Peripheral arthritis, n (%)	213(33.39)	107(26.55)	106(45.11)	<0.001
History of LBP, n (%)	534(83.70)	353(87.59)	181(77.02)	<0.001
Family history of SpA, n (%)	62(9.72)	34(8.44)	28(11.91)	0.153
History of IBD, n (%)	11(1.72)	6(1.49)	5(2.13)	0.55
History of psoriasis, n (%)	21(3.29)	9(2.23)	12(5.11)	0.05
HLA-B27, n (%)	521(81.66)	351(87.10)	170(72.34)	<0.001
Drug use information, n (%)				
bDMARDs	167(26.18)	129(32.01)	38(16.17)	<0.001
NSAIDs	420(65.83)	273(67.74)	147(62.55)	0.183
csDMARDs	145(22.73)	98(24.32)	47(20.00)	0.21
CRP at baseline (mg/L)	11.56±22.41	12.89±23.13	9.27±20.98	0.098
ASDAS-CRP	2.60±1.21	2.60±1.25	2.60±1.18	0.82
BASDAI	3.40±1.99	3.17±2.08	3.88±1.73	0.362
BASFI	1.99±2.64	2.09±2.70	1.77±2.55	0.798
BASMI	2.11±2.44	2.66±2.49	0.95±1.91	0.196

Notes: Male, History of LBP, Peripheral arthritis, Family history of SpA, History of IBD, History of psoriasis, HLA-B27, Drug used information tested by $\chi 2$ test. Age at enrollment, Symptom duration at first visit, CRP at baseline, ASDAS-CRP, BASDAI, BASFI, BASMI used *t*-test.

Table 4 Sensitivity and Specificity of CRP for Disease Activity Using MRI as the Gold Standard

Variables	MRI (axSpA Group)		MRI (AS Group)		MRI (Nr-SpA Group)	
	Se (%)	Sp (%)	Se (%)	Sp (%)	Se (%)	Sp (%)
BME	42.58	66.42	47.13	58.49	33.33	77.39
Erosion	42.52	65.66	42.86	50.77	41.18	77.25
Fat metaplasia	47.06	63.2	47.12	55.85	46.67	80.5
Backfill	52.34	64.03	52.58	57.52	50	72.89
Ankylosis	63.83	60.84	63.83	60.84	Nil	Nil

40% to 66%. In the AS group, neither sensitivity nor specificity exceeded 60%. In the nr-axSpA group, sensitivity remained below 50%, whereas specificity ranged between 70% and 80% (Table 4).

Discussion

This study found that even when markers such as CRP are normal, MRI remains a powerful tool for assessing disease activity in axSpA. Current approaches to evaluating axSpA disease activity do not incorporate imaging tools like MRI. However, in clinical practice, physicians may encounter patients with normal disease activity assessments who still experience symptoms such as low back pain or morning stiffness. In such cases, additional assessment tools are needed. Our data suggest that MRI findings should be integrated into the process of evaluating axSpA disease activity.

Following the introduction of the axSpA classification criteria in 2009, advances in MRI technology have facilitated the identification of a greater number of individuals with axSpA. This development has supported earlier therapeutic intervention and contributed to a reduction in late-stage joint ankylosis. On standard MRI sequences, including T1-weighted imaging (T1WI) and fat-suppressed T2-weighted or short tau inversion recovery (T2WI-FS/STIR), sacroiliitis

is characterized by both active lesions (eg, BME, enthesitis, and capsulitis) and structural lesions (eg, erosion, sclerosis, ankylosis, and fat metaplasia). Among these, the Assessment of SpondyloArthritis international Society (ASAS) currently considers only BME as a criterion for a "positive MRI" in the diagnosis of sacroiliitis associated with spondyloarthritis (SpA). Nevertheless, accumulating evidence from MRI specialists and rheumatologists has indicated that the concurrent presence of active and structural lesions may enhance the positive predictive value (PPV) and positive likelihood ratio (LR+) for the diagnosis of SpA.[6,18,19]

To date, studies evaluating SIJ or spinal MRI for assessing axSpA disease activity remain ongoing, with varying perspectives among researchers. Inan et al found that among HLA-B27-negative axSpA patients, only the SPARCC score showed a strong positive correlation with BASDAI. In the overall patient population and among HLA-B27-positive patients, no significant correlation was observed between clinical indicators such as BASDAI, ASDAS scores, ESR, and CRP and the SPARCC score. Therefore, they concluded that SIJ MRI is not necessary for routine monitoring of disease activity. However, Inan et al's study included only 32 SpA patients and assessed MRI solely for BME, presenting certain limitations.[20]

CRP, ESR, and ASDAS-CRP indices are commonly used for the clinical assessment of disease activity in axSpA. First, given that ASDAS-CRP is primarily employed in clinical research, CRP is more frequently utilized in clinical practice to assess disease activity, and the relationship between ASDAS-CRP and MRI has been substantiated in prior studies.[21] Second, ESR is not easily comparable due to variations in standards employed by different laboratories and between genders. In contrast, CRP is a stable method with consistent normal values across various centers and no gender differences. To reflect the actual clinical scenario in which healthcare providers evaluate inflammation in patients, this study selected CRP and MRI.

In this study, patients with axSpA at both the initial stage of treatment and those who had been previously treated were included. MRI imaging and CRP levels were investigated during the same examination period. As commonly observed in clinical practice, CRP is considered a non-specific indicator of inflammation, with elevated levels signifying disease activity, while MRI provides insight into the presence of inflammation in the sacroiliac joints. Current consensus in the literature suggests that nr-axSpA represents the early stage of the axSpA disease spectrum, whereas AS is considered the later stage of the SpA disease spectrum. Nr-axSpA is more likely to reach normal CRP levels following treatment, which explains why the proportion of nr-axSpA in the normal CRP group is significantly higher than in the abnormal CRP group. Additionally, it was found that the proportion of male participants in the normal CRP group was significantly lower than in the abnormal CRP group, possibly due to the fact that females with axSpA tend to experience milder disease and are more likely to achieve low disease activity.

The results of this study indicate that MRI features, including BME, erosion, fat metaplasia, backfill, and ankylosis, differ significantly between the normal and abnormal CRP groups. These findings indicate that MRI can effectively reflect disease activity in axSpA, independent of CRP levels. Even in cases where CRP is normal, MRI revealed 53.45% BME, 50.13% erosion, 16.11% fat metaplasia, 13.04% backfill, and 8.7% ankylosis. Therefore, MRI can be utilized as a valuable tool for assessing disease activity in axSpA, even when CRP levels are within the normal range.

Previous studies have indicated that when patients with axSpA achieve low disease activity, active sacroiliitis on MRI and anti-TNF-α therapy should be considered in assessing remission and potential disease flare-ups.[6] The study also indicates that nr-axSpA and AS share similar characteristics regarding age, HLA-B27 positivity rate, incidence of peripheral arthritis and extra-articular symptoms, and disease activity.[22] However, compared to nr-axSpA, AS is associated with a higher prevalence of male patients and significantly elevated CRP levels. A post-hoc analysis revealed that the proportion of male patients was lower, while the proportion of female patients higher among the nr-axSpA cohort in this study. Specifically, the ratio of female patients in the nr-axSpA group was significantly higher than in the AS group. Given that nr-axSpA is predominantly diagnosed through MRI, which requires interpretation by experienced MRI and rheumatology specialists, the hospital, as a tertiary care facility, receives most difficult-to-diagnose cases, introducing potential selection bias at the time of admission and contributing to the higher proportion of female patients.

Similarly, due to the challenges in diagnosing nr-axSpA based on peripheral arthritis, patients are often referred to the outpatient clinic. Previous research has indicated that the incidence of peripheral arthritis in patients with AS ranges from 22% to 70%, while in patients with nr-axSpA, it varies between 47.3% and 73.6%, which aligns with the findings in the

current study.[23,24] In this study, the HLA-B27 positivity rate in the AS group was significantly higher than in the nr-axSpA group. Given that the diagnosis of nr-axSpA does not depend on HLA-B27, it can be confirmed if other SpA characteristics, such as low back pain, age, and MRI findings are present, which explains the lower HLA-B27 positivity rate in the nr-axSpA group.

Wang et al summarized the histopathological progression of sacroiliitis in AS that it began with inflammation of the synovium and subchondral bone marrow, leading to cartilage degeneration and subsequent destruction of subchondral bone.[25] This process ultimately results in endochondral ossification and the formation of bony bridges. Although nr-axSpA is traditionally considered the early phase of the axSpA disease spectrum, continuous MRI-based tracking across early, intermediate, and late stages of axSpA has not been substantiated by high-quality clinical evidence and remains largely speculative. Current consensus suggests that MRI lesions may evolve through a sequence involving BME, erosions, fat metaplasia, backfill, and ankylosis.

The 2015 EULAR recommendations for the use of imaging in the diagnosis and management of spondyloarthritis in clinical practice indicate that MRI imaging of the sacroiliac joints or spine can provide additional information beyond biochemical and clinical assessments to demonstrate disease activity in spondyloarthritis. However, they do not specify how frequently MRI should be repeated to monitor structural changes in axSpA.[26]

James et al investigated the relationship between MRI findings and BASDAI, ASDAS-CRP, and ASDAS-ESR scores in 40 patients with axSpA. They found no significant correlation between SPACC scores and DAS scores, nor between SPACC scores and ASDAS scores.[27]

Current studies have not identified a relationship between CRP and axSpA disease activity, potentially due to the inclusion of subjective symptoms and laboratory tests in disease activity assessment criteria. For individuals with clinical symptoms but normal CRP levels, CRP does not effectively reflect disease activity. Furthermore, current disease activity assessment criteria do not incorporate imaging studies. For axSpA patients who exhibit no subjective symptoms and normal CRP but show active inflammation detectable by MRI, current evaluation methods may yield false negatives. Discontinuing medication may lead to disease recurrence.

Most current studies have not identified a correlation between CRP and SIJ MRI findings. Furthermore, SPARCC scoring is based solely on MRI-assessed BME, presenting certain limitations, and the sample sizes remain relatively small.

Therefore, this study aims to investigate the relationship between the clinically common markers CRP and MRI in axSpA, while also evaluating structural lesions (erosions, sclerosis, fat metaplasia, and ankylosing) on MRI, as well as the co-occurrence of active and structural lesions on MRI.

This study found that MRI remains a valuable tool for assessing disease activity in axSpA even when CRP levels are normal. We recommend that sacroiliac joint MRI be repeated to evaluate disease activity in axSpA patients, even in the absence of low back pain symptoms and with normal CRP levels.

Post hoc analysis indicated that individuals with axSpA and elevated CRP levels were more likely to exhibit both active and structural inflammation on MRI. Statistically significant differences were observed in the distribution of MRI-detected lesions between the AS and nr-axSpA groups, with the AS group exhibiting a higher incidence of active and structural abnormalities. These findings support the conceptualization of nr-axSpA as an earlier stage and AS being a more advanced stage within the axSpA continuum.

Further subgroup analysis based on CRP stratification within the AS and nr-axSpA groups provided additional insights. In the AS group, no statistically significant differences in active or structural lesions were noted between normal and elevated CRP subgroups, with the exception of ankylosis. Among individuals with AS, erosion was the most prevalent lesion, followed by BME, whereas fat metaplasia, backfill, and ankylosis occurred less frequently. These findings indicate that the development of structural lesions in axSpA may not be entirely dependent on systemic inflammatory activity, as reflected by CRP levels. The relative frequencies of lesions imply a progression in AS pathophysiology: early stages marked by inflammation (ie, BME) and structural breakdown (ie, erosion), followed by reparative changes (ie, fat metaplasia and backfill), and culminating in ankylosis. However, as this study is neither a prospective nor a longitudinal one, but only a retrospective analysis, it is currently unable to provide continuous

imaging over time. The existing data can only indirectly suggest the above sequence. The actual situation still needs to be confirmed by further observational studies.

In the nr-axSpA group, statistically significant differences in MRI-detected erosions across CRP subgroups indicate that erosion may represent an intermediate stage, bridging active inflammation and more advanced structural damage. Although it is conventionally proposed that MRI lesions follow a progression from BME to fat metaplasia to ankylosis, current data do not confirm this sequence. Ankylosis was absent on MRI in the nr-axSpA group, aligning with the diagnostic criteria for nr-axSpA and supporting the internal validity of the data. Moreover, the co-occurrence of BME and structural lesions in both CRP-defined nr-axSpA subgroups was statistically significant, potentially indicating that MRI is more effective for identifying early axSpA, particularly in the nr-axSpA stage.

In the nr-axSpA group, the CRP-abnormal subgroup demonstrated a higher likelihood of exhibiting BME compared to the CRP-normal subgroup, although the p-value of 0.068 was close to the conventional threshold of 0.05. Whether statistical significance could be achieved with a larger sample remains uncertain and warrants confirmation through future investigations with expanded datasets.

CRP has been widely adopted in clinical settings as one of the most common tools for assessing disease activity in axSpA. Although advancements in MRI technology have enhanced its utility in diagnosing axSpA, its application in evaluating disease activity remains limited. Given that MRI is the only non-invasive imaging modality capable of detecting lesions such as BME, MRI was employed in this study as the reference standard for evaluating the sensitivity of CRP in identifying disease activity. Findings indicated that CRP was less effective than MRI in detecting disease activity in axSpA, indicating that MRI serves as a more reliable modality in clinical assessment.

Although CRP, ESR, and ASDAS indices are routinely employed for clinical evaluation of axSpA, the ASDAS scale is infrequently used in some medical centers. Furthermore, ASDAS scoring requires integration with CRP or ESR values. ESR values are subject to variability across laboratories and exhibit sex-based differences, rendering direct comparisons challenging. In contrast, CRP provides a more stable measurement, with consistent reference values across centers and no gender-specific variation. As a non-specific inflammatory marker, CRP is widely used in clinical settings, though its sensitivity and specificity in detecting axSpA disease activity are inferior to those of MRI. Thus, a multimodal approach that incorporates both MRI and laboratory indicators is recommended for comprehensive clinical assessment.

This study has several limitations. First, the inclusion of only patients who presented to a single tertiary care center introduces the potential for admission selection bias (Berkson bias) and detection bias. Some patients with LBP may have sought care in orthopedic or pain clinics, potentially contributing to a lower detection rate of nr-axSpA and a reduced number of patients in this group completing MRI scans, thereby inflating the proportion of AS diagnoses. Additionally, the referral pattern to this tertiary hospital, equipped with a radiology department experienced in diagnosing sacroiliitis, may have further contributed to selection bias by increasing the proportion of diagnostically complex cases. Second, due to incomplete medical histories, some patients with early-stage LBP may have delayed clinical consultation until the development of spinal deformities, contributing to underdiagnosis of nr-axSpA. Third, this study evaluated MRI and CRP data from a single time point and did not account for previous treatments, which may represent a confounding factor.

However, due to limitations in sample size, further subgroup analyses were not performed. Different treatment exposures may influence the types of acute and chronic lesions detected by MRI. However, since this study did not analyze treatment status for axSpA, an increased incidence of chronic lesions may be observed.

Since this study is not a prospective or longitudinal study but rather a retrospective analysis, the existing data can only indirectly suggest the aforementioned sequence.Further research is needed to confirm the actual situation.MRI and CRP were assessed at a single time point and that longitudinal evaluation might alter lesion detection rates.

Conclusion

The findings of this study indicate that CRP and MRI can be used in combination to assess disease activity in axSpA. In cases where CRP levels are within normal range, MRI serves as a valuable imaging modality for detecting active disease. Furthermore, the data indirectly prompted support a sequential pattern of lesion development in axSpA, progressing from BME to erosion, followed by fat metaplasia, backfill, and ultimately ankylosis. The results also reinforce the conceptual

framework in which nr-axSpA represents an earlier stage of the disease, while AS corresponds to a more advanced stage of axSpA.

Abbreviations

axSpA, axial spondyloarthritis; MRI, Magnetic resonance imaging; AS, ankylosing spondylitis; nr-axSpA, non-radiographic axial spondyloarthritis; ASDAS-CRP, Ankylosing Spondylitis Disease Activity Score based on C-reactive protein; CPR (cardiopulmonary resuscitation; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASMI, Bath Ankylosing Spondylitis Metrology Index; BASFI, Bath Ankylosing Spondylitis Functional Index; ESR, erythrocyte sedimentation rate; SIJs, sacroiliac joints; NSAIDs, nonsteroidal anti-inflammatory drugs; csDMARDs, conventional synthetic Disease-Modifying Anti-rheumatic Drugs; bDMARDs, biological Disease-Modifying Anti-Rheumatic Drugs; HLA-B27, Human leucocyte antigen B27; SPARCC, Spondyloarthritis Research Consortium of Canada; BME, bone marrow edema; PPV, positive predictive value; LBP, low back pain.

Data Sharing Statement

The data that support the findings of this study are available from Qing Zheng upon reasonable request.

Ethics Approval and Consent to Participate

The investigation was sanctioned by the the Ethics Committee of the First Affiliated Hospital of Fujian Medical University (Approval No. MRCTA, FMU ECFAH[2018]198). This study was conducted in accordance with the declaration of Helsinki. Written informed consent was obtained from all patients.

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Disclosure

The authors declare that they have no competing interests.

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