Magnetic Resonance Imaging role in assessment of axial spondylarthritis Disease activity and Severity

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Abstract

Background: Imaging has a central role in the diagnosis, management, and follow-up of patients with axial spondyloarthritis (axSpA). For the early diagnosis of axSpA, magnetic resonance imaging is of utmost relevance. While no novel imaging techniques were developed during the past decade, improvements to the existing modalities have been introduced. When it comes to axial spondyloarthritis (SpA), magnetic resonance imaging (MRI) is one of the most sensitive imaging modalities for detecting early inflammatory changes. It has been more than ten years since the ASAS classification criteria for axial SpA, which were last updated in 2009, included magnetic resonance imaging (MRI) evaluation. Within that time, a mountain of evidence and clinical experience with magnetic resonance imaging (MRI) in axial SpA has quickly been built up. Early diagnosis, assessment of disease activity, and tracking of therapy response in axial SpA have all been improved by this improved understanding of the clinical value of MRI. Innovations in technology have also allowed for the creation of new magnetic resonance imaging (MRI) sequences that can optimize images and quantify inflammation.

Keywords: axial spondylarthritis, Magnetic Resonance Imaging

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Introduction:

Spondyloarthritis (SpA) describes a group of inflammatory conditions with ankylosing spondylitis (AS) as the protype disease.[1] The spectrum is represented by AS on one end and non-radiographic SpA on the other end, where established radiographic sacroiliitis is evident on conventional radiographs in the former and absent in the latter. It is known that inflammation and early

structural changes may occur long before established changes are evident on conventional radiographs.[2] The development of effective treatments has called for strategies to aid early diagnosis. Magnetic resonance imaging (MRI) is a sensitive imaging modality to detect active inflammation in the axial skeleton. A correlation between MRI lesions and histological features have also been shown.[3] Over the past decades, MRI has established its valuable roles in axial SpA. Evidence and clinical experience of MRI in early diagnosis and disease activity assessment have been accumulating, and continued progress has been made in the development of novel MRI sequences.

A better understanding of the broader spectrum of diseases caused by axSpA has been encouraged by this notion and the ASAS categorization criteria [4]. Because of the difficulty in conducting clinical examinations of the SIJs and the high degree of symptom overlap between inflammatory and mechanical back pain, imaging of the SIJs is crucial for the early diagnosis of axSpA, since the majority of patients exhibit SIJ involvement. In most cases, spinal abnormalities indicate a more advanced stage of the illness. Spinal abnormalities independent of SIJ alterations are observed in a small subset of AS patients [5]. So yet, no criteria for classifying axSpA have included spinal involvement. Inflammatory, osteodestructive, or osteoproliferative alterations in the spinal intervertebral joints (SIJs) and spine are hallmarks of axSpA. New bone development, such as syndesmophytes and ankylosis, follows the inflammatory symptoms of sacroiliitis, spondylitis, aseptic spondylodiscitis, and inflammation of the posterior components of the spine in axSpA [6-8]. Numerous methods for diagnosing, classifying, evaluating disease activity, structural damage, and prognosis of axSpA patients have been developed thanks to significant advancements in the field of imaging in the previous several decades. But CR is still the go-to for determining the extent of structural damage in axSpA patients. If you're looking for active inflammatory alterations that CR and CT can't pick up on, magnetic resonance imaging (MRI) is your best bet. There are a number of additional imaging modalities that can be used to confirm axSpA, although they are not generally advised for this purpose. Instead, they should be utilized in conjunction with one another and as needed.

Mri For Early Detection, Diagnosis, And Classification Of Axial Spa

Early detection of sacroiliitis and classification of axial SpA

When diagnosing AS, radiographic sacroiliitis is the most important imaging finding, and the modified New York criteria have been utilized extensively.[4] A In cases of axial SpA, a recent systematic study found a diagnosis delay of 0.67 to 8 years.[5] The early diagnosis of axial SpA has been made possible by magnetic resonance imaging (MRI), which can reveal inflammation prior to the formation of structural abnormalities. The European Spondyloarthropathy Study Group and the Amor criteria are two examples of the many proposed classification systems that have evolved throughout time..[6, 7] Classification criteria were designed to select homogenous patients for research purposes and should only be applied to patients with an established diagnosis of axial

SpA. The Assessment of SpondyloArthritis International Society (ASAS) classification criteria for axial SpA were developed in 2009 and included a clinical arm and an imaging arm.[8] Patients are classified into the "imaging arm" in the presence of sacroiliitis by radiography or by MRI plus at least one SpA feature, or the "clinical arm" in the presence of HLA-B27 plus at least two SpA features. According to the ASAS criteria, positive MRI sacroiliitis was defined as (1) the presence of definite bone marrow edema/osteitis highly suggestive of sacroiliitis, (2) located in the typical anatomical areas (subchondral or periarticular bone marrow), and (3) meeting the required amount of signal (at least two consecutive slices if only one signal per MRI slice; one slice may be sufficient if more than one signal per slice).[9] The overall performance of the imaging arm (±clinical arm) of the ASAS criteria for axial SpA was reported to have a pooled sensitivity of 57% and a specificity of 96%.[10] A study based on longitudinal data from the Devenir des Spondyloarthropathies Indifférenciées Récentes (DESIR) cohort (a large national multicenter cohort of patients with early inflammatory back pain of more than 3 months and less than 3 years) demonstrated excellent predictive validity of the ASAS criteria at baseline assessment when tested against the rheumatologist's diagnosis of axial SpA.[11] The results highlight the utility of the ASAS criteria among patients with early disease onset.

MRI also serves as one of the imaging modalities in juvenile SpA.[12] Similar to adults with SpA, MRI can detect sacroiliitis in juvenile SpA before changes are present in radiographs.[13] In a prospective cross-sectional study of 40 children with newly diagnosed juvenile SpA, active MRI sacroiliitis was found in 20% of patients, and most cases were asymptomatic.[14] Gadolinium contrast may be considered in selected patients to detect synovitis, which may occur in the absence of bone marrow edema, after weighing against possible contrast-related side effects such as injection-site discomfort and hypersensitivity.[15] More research is needed to define and standardize the best approach to imaging and the role of MRI in children with juvenile SpA.[16]

MRI interpretation in SpA and mimickers of sacroiliitis

With the advent of MRI, axial SpA can now be detected earlier. Bone marrow edema lesions can appear on magnetic resonance imaging (MRI), although they can also be seen in plenty of healthy people. One study indicated that 57.1% of postpartum mothers, 16.7% of runners, and 25.5% of healthy adults had positive MRI sacroiliitis, using the Spondyloarthritis Research Consortium of Canada (SPARCC) score of ≥2 as the criterion.[17] Mechanical stress on the sacroiliac joint has been proposed as an underlying mechanism, but it does not fully account for the development of bone marrow edema.[18] The extent and anatomical distribution of bone marrow edema lesions may provide useful information. Deep bone marrow edema lesions (defined as a homogenous, unequivocal increase in signal at least 1 cm from the articular surface) were more specific among patients with axial SpA (Figure 1).[17] Furthermore, bone marrow edema lesions occur more frequently in the intermediate-middle segment in axial SpA and predominantly affect the antero-middle segment in non-SpA participants (Figure 2). Bilateral bone marrow edema lesions are more common in SpA compared with non-SpA, except for women with postpartum back pain.[19] Given

the high prevalence of non-specific bone marrow lesions among non-SpA patients, MRI should be interpreted based on the contexts of individual patients, considering various clinical and serological features, to avoid overdiagnosis of axial SpA.[20]

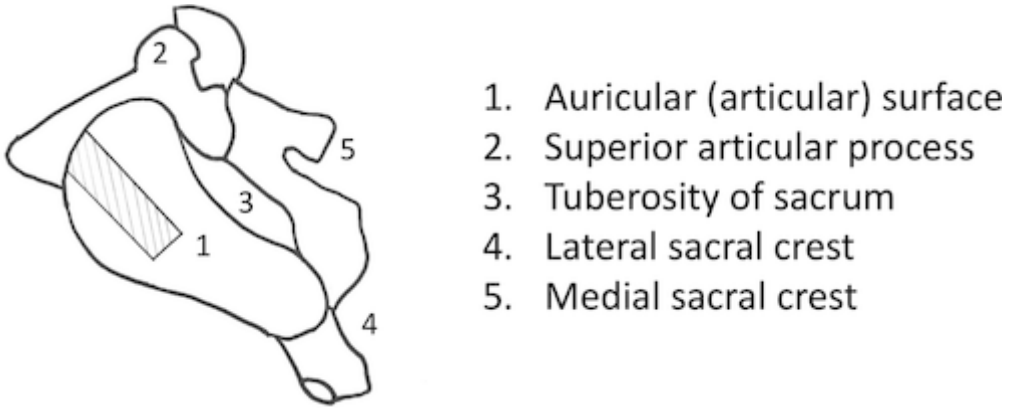

Figure 1: Bilateral sacroiliitis on short tau inversion recovery magenetic resonance imaging. Deep bone marrow edema lesions (defined as a homogenous, unequivocal increase in signal at least 1 cm from the articular surface) are shown in bilateral sacroiliac joints (white arrows).

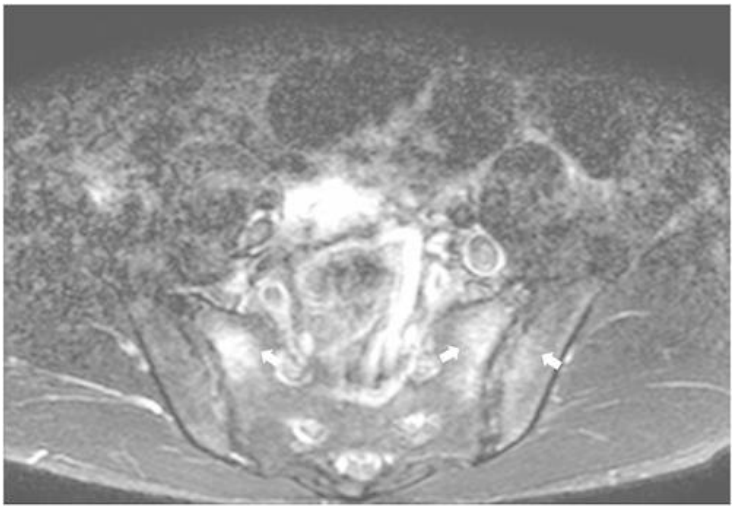

Figure 2: The intermediate-middle segment of the sacroiliac joint that is predominantly affected in axial spondyloarthritis.

Utility of sacroiliac joint structural lesions and spinal MRI in axial SpA

In addition to bone marrow edema, different MRI inflammatory and structural lesions of the sacroiliac joint have been defined.[8] Structural lesions in the sacroiliac joint include erosions, periarticular fat depositions, and ankylosis. Several studies have examined the role of structural lesions in the classification of axial SpA. A proposed cutoff of erosions ≥3, fatty lesions ≥3, or erosions/fatty lesions ≥5 (based on <5% prevalence among non-SpA patients) was evaluated in previous studies and demonstrated good performance either as an addition to or as a substitute for radiographs in the ASAS axial SpA classification[21]; further studies are needed to confirm its usefulness in clinical practice. A recent study carried out by the ASAS MRI group proposed data-

driven definitions of active and structural lesions of the sacroiliac joints in SpA, defined as achieving a positive predictive value of ≥95%.[22] Either bone marrow edema in ≥4 quadrants at any location or at the same location in ≥3 consecutive slices contributed to the best cutoffs for a definite active lesion typical of axial SpA. The optimal cutoffs for definite structural lesion included ≥3 quadrants with erosion or ≥5 with fat lesions, erosion at the same location for ≥2 consecutive slices, fat lesions at the same location for ≥3 consecutive slices, or the presence of a deep (defined as >1 cm depth) fat lesion.

Since the inflammatory process in axial SpA does not limit itself to the sacroiliac joint and may affect different spinal segments, several studies have evaluated the diagnostic utility of spinal MRI in axial SpA. The presence of ≥3 corner inflammatory lesions (CILs) has been proposed as the definition of a positive spinal MRI for axial SpA by the ASAS/Outcome Measures in Rheumatology working group.[23] Earlier studies have shown that when used alone, whole-spine CILs have poor diagnostic utility.[24] Spinal MRI also adds little incremental diagnostic value when added to sacroiliac joint MRI assessment.[24] A study has shown that among patients without sacroiliitis on MRI or radiographs, 8%–13% might be diagnosed by spinal MRI.[25] Thoracic and whole spine MRI had similar diagnostic performance using the proposed cutoff of ≥5 whole spine CILs and ≥3 thoracic spine CILs.[25] In a study of 238 patients with axial SpA, it was shown that ≥3 fatty corner lesions (FCLs) in T1-weighted MRI could be used for diagnosis without additional MRI sacroiliac joints.[26]

Mri For Disease Activity Assessment

Correlation between clinical disease activity index and MRI inflammation

Reliable biomarkers for axial SpA are still few. Although it does not specifically identify axial SpA, HLA-B27 is a helpful marker that indicates a poor prognosis. In standard clinical practice, patients with axial SpA often have clinical disease activity indices like BASDAI and ASDAS administered to them to assess disease activity.[27, 28] BASDAI is a self-score index that includes fatigue, pain (in axial and peripheral joints), swelling, and the level and duration of morning stiffness. The ASDAS is a composite index that is also based on a similar set of subjective symptoms, including back pain, duration of morning stiffness, patient global assessment, and peripheral pain and swelling. In addition to self-rated parameters, ASDAS also includes serum inflammatory markers, namely C-reactive protein (CRP) or erythrocyte sedimentation rate (ESR), which serve as an objective measure of inflammation.

Inflammation on MRI has been shown to be correlated with inflammatory cellularity documented by tissue biopsy.[29] Therefore, researchers are using MRI as a “gold standard” for comparison. Traditional inflammatory markers, including CRP and ESR, correlate poorly with MRI-detected inflammation.[30] Many studies have found conflicting results regarding the correlation between clinical disease activity indices and MRI inflammation. Two-year data from the DESIR cohort demonstrated a significant association between MRI inflammation in the sacroiliac joint and

ASDAS in male patients but not in female patients.[31] In a study of 149 patients with axial SpA, Byravan et al.[32] reported a significant correlation between active sacroiliitis and BASDAI. However, the study showed no correlation between BASDAI and other MRI features including, chronic sacroiliitis, active axial disease, and other MRI changes (costovertebral, costotransverse, and sternoclavicular inflammation). Another study showed that ASDAS was associated with both the extent and intensity of spinal inflammation in patients with detectable MRI inflammation only.[33] An MRI of the SI joint and/or the spine may be considered based on the physician's discretion to complement clinical and biochemical assessment at the initial stage and to provide an objective assessment of activity for disease monitoring.[34, 35]

MRI inflammation as predictors for treatment response to biological therapies

When deciding on a course of treatment, MRI is also crucial. Patients diagnosed with axial SpA by a rheumatologist who do not respond to standard therapy are advised to consider biological therapies..[36] Given the treatment costs and potential side effects, careful selection of patients who would benefit most from biological therapies remains important. Studies based on data from randomized controlled trials have shown that the presence of SI and spinal inflammation on MRI was associated with a higher likelihood of treatment response with TNF inhibitors.[37] Other predictive factors of response to TNF inhibitors included shorter disease duration, HLA-B27 positivity, and raised CRP. Similar findings have been shown with anti-IL17 treatment.[38] Based on the evidence, it is recommended that patients considered for biological therapies should have elevated CRP, the presence of inflammation on the MRI SI joint, or radiographic sacroiliitis at baseline before treatment initiation.

MRI also serves as an objective assessment of treatment response. A recent systematic review and meta-analysis evaluated the differences in MRI changes in SpA patients treated with anti-TNF agents compared with patients without biological treatment.[39] Based on the SPARCC score, a significant difference in reduction of MRI sacroiliac joint inflammation among patients treated with TNF inhibitors was found. A tendency toward reduction of MRI spinal inflammation was also observed among patients treated with TNF inhibitors, even though it did not reach statistical significance. Furthermore, reductions in MRI inflammation demonstrated a correlation with improvements in clinical disease activity indices in most of these studies.

Potential roles of MRI in determining treatment targets in SpA

The management of various rheumatological disorders has been impacted by the rise of the treat-to-target (T2T) strategy. Remission of disease or low disease activity, prevention of disease consequences and treatment-related adverse effects, and improvement of functional outcomes for patients are often the goals of treatment. Remission in rheumatoid arthritis has been defined in T2T using both index-based and Boolean criteria..[40] Compared with RA, a T2T treatment strategy in SpA is less extensively evaluated. A set of recommendations for treatment targets in axial SpA and peripheral SpA was formulated in 2017.[41] Clinical remission or inactive disease (defined as

ASDAS <1.3 in axial SpA) was recommended as the treatment target. Low or minimal disease activity (defined as ASDAS <2.1) may be an alternative treatment target. However, a randomized trial evaluating the efficacy of the T2T approach in axial SpA failed to demonstrate a significant difference in the primary endpoint between the T2T arm and the usual care arm.[42] Treatment intensification and biologic prescriptions were more frequent in the T2T arm.

Since MRI provides a valuable objective measure of inflammation and predicts treatment response to biological therapies, it remains to be answered whether there is a role for MRI assessment in determining treatment target in axial SpA. The frequency of clinical and MRI remission was compared based on the 3-year results of the ABILITY-1 trial, a randomized controlled trial evaluating adalimumab in non-radiographic axial SpA.[43] Among patients with positive MRI who achieved ASAS inactive disease, only 40% and 44% achieved MRI remission (both in the sacroiliac joint and spine) at years 1 and 2, respectively. A study by Zheng et al.[44] evaluated the frequency and predictive value of the flare of MRI-active sacroiliitis among patients in clinical remission. Active MRI sacroiliitis, found in 55.8% of patients in clinical remission, was associated with a significant risk of disease flare. Further studies are anticipated to evaluate the impact of persistent MR inflammation on long-term physical function or structural progression among axial SpA in clinical remission. It remains to be answered whether MRI plays a role in complementing clinical disease activity in determining treatment targets in axial SpA.

Novel Mri Sequences

This review focuses on a handful of the many innovative MRI sequences that have been tested over the years. One way to measure the severity of inflammation is via diffusion-weighted imaging (DWI) and the apparent diffusion coefficient (ADC)..[45-48] Readout-segment echo-planar imaging (EPI) and intravoxel incoherent motion diffusion-weighted imaging (IVIM-DWI) have been evaluated to improve DWI image quality.[49, 50] Whole-body MRI (WBMRI) assesses the inflammatory activities of the entire musculoskeletal system.[46-48] Volumetric interpolated breath-hold examination (VIBE) demonstrated better sensitivity at detecting erosive damage in the sacroiliac joint.[51] These imaging sequences have been mainly evaluated in research settings, and further studies are needed to delineate their roles in clinical practices.

Diffusion-weighted imaging

Using the Brownian motion of water molecules as its basis, DWI is a new MRI sequence. DWI has found extensive use in the assessment of intracranial disorders, including trauma and cerebrovascular illnesses. A growing number of extra-cranial disorders, such as those affecting the muscles and joints, are also being investigated using DWI. The usefulness of DWI for diagnosing axial SpA and sacroiliitis has been the subject of multiple investigations. In a study involving 305 individuals suffering from back pain, the diagnostic value of DWI was assessed.[45] DWI and STIR demonstrated similar sensitivity in diagnosing axSpA in early disease. Despite its comparable sensitivity to STIR, the limited resolution of DWI rendered its poorer reliability. The addition of

DWI to conventional MRI of the sacroiliac joint did not improve the overall diagnostic performance except for increased specificity and interobserver agreement.[46]

Recently, an attempt to improve the image quality of DWI was made by using readout-segment EPI over the conventional single-shot EPI. In a study of 75 patients showed that readout-segment EPI had better image quality and diagnostic confidence compared with conventional single-short EPI.[49] Furthermore, the apparent diffusion coefficient (ADC) derived from readout-segment EPI had better discriminatory performance between different activity states of sacroiliitis compared with single-short EPI. However, ADC values from single-short EPI and readout-segment EPI vary across vendors, field strengths, and *b*-values. More studies are needed to confirm the role of readout-segment EPI in quantifying inflammation in sacroiliitis. Another DWI technique, IVIM-DWI, has also been explored in SpA. IVIM-DWI is a double exponential model based on the fitting of multiple *b*-values. IVIM-DWI has the ability to assess the diffusion of water molecules and perfusion separately.[50] IVIM-DWI allows tissue characterization based on perfusion patterns to distinguish between physiologic and pathologic conditions. In a study of 56 participants with AS, Liu et al.[50] demonstrated the superiority of IVIM-DWI over traditional DWI for the identification of different AS disease activity levels with a good correlation with the SPARCC score at the SI joints.

The assessment of spinal inflammation also contributes to the overall disease activity assessment. Based on conventional MRI sequences, such as short tau inversion recovery (STIR) and fat saturation sequences, different scoring methods have been developed to quantify the extent of inflammation, including the SPARCC MRI index, the ankylosing spondylitis spine MRI score for activity, or ASspiMRI-a, and the Berlin method.[52, 53] However, these scoring methods focused on the extent of inflammation without considering the intensity of inflammation in individual lesions. The SPARCC method only semi-quantitatively grades the degree of inflammation. ADC is a measure of the magnitude of the diffusivity of water molecules within tissues and has been explored to provide information on the intensity of inflammation in SpA. In a study of 243 participants with SpA, the maximum ADC of active discovertebral lesions (defined on STIR images as hyperintense bone marrow signal contiguous with the vertebral endplates with or without involvement of the vertebral corner in any central sagittal section) were shown to be associated with back pain intensity, functional impairment (measured by the Bath Ankylosing Spondylitis Functional Index), and patient global assessment.[47] ADC also correlates with clinical disease activity and spinal mobility (measured by ASDAS and BASMI, respectively).[48] Strategies to overcome the low-spatial resolution of DWI may improve the overall applicability of ADC in disease assessment in SpA.

Whole-body MRI

When inflammation occurs in SpA, it can spread beyond the axial skeleton and affect other parts of the musculoskeletal system, including the entheses and peripheral joints. Whole-body magnetic

resonance imaging (WBMRI) has been tested for use in evaluating inflammatory processes across the musculoskeletal system. The efficacy of biological therapy in SpA patients has been evaluated in a number of studies using WBMRI.[54-56] Different indices have been proposed based on WBMRI inflammation. The WBMRI indices measure peripheral joint inflammation, enthesitis, and axial inflammation of the spine and sacroiliac joints. WBMRI has the unique advantage of providing a comprehensive assessment of inflammation across different domains of musculoskeletal involvement in one single scan.

Conclusion

When it comes to axial SpA, MRI is a crucial for diagnosing and monitoring disease activity. This is especially helpful prior to beginning biologic therapy.

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