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Recommendations for Acquisition and Interpretation of MRI of the Spine and Sacroiliac Joints in the Diagnosis of Axial Spondyloarthritis in the UK

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Abstract

Aim: To develop evidence-based recommendations on the use of magnetic resonance imaging (MRI) in the diagnosis of axial spondyloarthritis (axSpA).

Method: A working group comprising nine rheumatologists and nine musculoskeletal radiologists with an interest in axSpA was established, with support from the British Society of Spondyloarthritis (BRITSpA). Two meetings were held. In the first meeting, research questions were formulated. In the second meeting, the results of a Systematic Literature Review (SLR) designed to inform the recommendations were reviewed. An anonymised Delphi process was used to formulate the final set of recommendations. For each recommendation, the level of evidence and strength of recommendation was determined. The level of agreement was assessed using a 0-10 numerical rating scale.

Results: Two over-arching principles (OPs) were formulated, as follows: The diagnosis of axSpA is based on clinical, laboratory and imaging features (OP1), and patients with axSpA can have isolated inflammation of either the sacroiliac joints or spine (OP2). Seven recommendations addressing the use of MRI in the assessment of patients with suspected axSpA were formulated, covering topics including recommended sequences, anatomical coverage, acquisition parameters and interpretation of active and structural MRI lesions. The level of agreement for each recommendation was very high (range 8.8–9.8).

Conclusion: A joint rheumatology and radiology consensus on the acquisition and the interpretation of MRI in axSpA diagnosis was achieved, and a research agenda formulated. This consensus should help standardise practice around MRI and ensure a more informed, consistent approach to the diagnosis of axSpA.

Introduction

Axial spondyloarthritis (axSpA) is an umbrella term encompassing a group of chronic immune-mediated inflammatory diseases of the axial skeleton (1). This group includes patients with ankylosing spondylitis (AS), with established sacroiliitis on radiographs, and a further subgroup called non-radiographic axial SpA (nr-axSpA), who typically have evidence of sacroiliitis on MRI in the absence of definite radiographic change. Despite the absence of radiographic structural damage of the sacroliliac joints (SIJ), the burden of disease in non-radiographic axSpA is similar to that seen in radiographic axSpA (2). Historically, the diagnosis of axSpA has often been delayed since radiographic abnormalities may take years to develop. In recent years, the introduction of MRI into clinical practice has facilitated earlier diagnosis of axSpA, and therefore earlier initiation of appropriate treatment, which may encompass exercise, non-steroidal anti-inflammatory drugs (NSAIDs) and biologic drugs. There is also evidence that MRI can be used to monitor the burden of inflammation in patients on treatment (3) and may predict response to therapy (4), with the potential for improvement in long term outcomes.

Whilst the utility of MRI in axSpA has been widely accepted, recent work has demonstrated significant inconsistency in its use in clinical practice (5). In a survey, Bennett et al. found that only 75% of radiologists were aware of the term axSpA, and only 31% and 25% were aware of the ASAS definitions of positive MRI of the SIJ and spine, respectively (5). Despite being widely accepted as a key diagnostic marker (6,7), bone marrow oedema (BMO) was not used as a potential diagnostic feature of axSpA by 18% of radiologists (5). The heterogeneity around MRI protocols and image interpretation may contribute to inconsistency in diagnosis. As such, there is an unmet need for standardisation of MRI protocols and a consensus on how images should be interpreted to aid diagnosis of axSpA in clinical practice.

The aim of this project was to provide guidance on the acquisition and interpretation of MRI in the diagnostic evaluation of patients with suspected axSpA in the UK. These recommendations were designed for both rheumatologists and radiologists and may also be of value to other physicians and radiographers worldwide.

Materials and Methods

This project was endorsed by the British Society for Spondyloarthritis (BRITSpA) executive committee. The convenors (MHC, HMO and PMM) led a task force guided by the 2014 updated EULAR standardised operating procedures (8). The 18 task force members consisted of both rheumatologists (n=9) and musculoskeletal radiologists (n=9) with an interest in axSpA. All members disclosed their potential conflicts of interest. Two task force meetings took place.

At the first task force meeting, the panel agreed on three key questions relating to the use of MRI in the diagnosis of axSpA (Table 1). These questions were subsequently framed using the Patient, Intervention, Comparator, and Outcome (PICO) format (for further detail see SLR ref).

The systematic literature review (SLR) was carried out by two task force members (AJ and TJPB) under the guidance of the methodologist and lead convenor (PMM). The search strategy from a previous European League Against Rheumatism (EULAR) systematic review addressing the role of imaging in spondyloarthritis was adopted (9). MEDLINE, Embase and Cochrane databases were searched without language restrictions. All studies performed between January 2013 and March 2017 were included. In addition, relevant studies from the previous EULAR SLR, which included all studies from the inception of the databases up to January 2013, were included. Quality assessment of all relevant studies was done using the QUADAS-2 tool (10). Although the SLR informing these recommendations has been published separately (SLR ref), both the SLR and this manuscript form a single body of work and should be read as such.

At the second meeting, data from the SLR were categorised by research question and presented to the taskforce. The data presented included the main outcomes for each of the included studies, MRI acquisition parameters and the results of the quality assessment. The taskforce then formulated the draft recommendations based on the evidence and expert opinion in a process of discussion and consensus, followed by final voting on the recommendations. The wording of the recommendations was refined and finalised by email exchange.

An anonymised Delphi process was used to formulate the final set of recommendations. For each recommendation, consensus was accepted if >75% of members voted in favour in the first round, if >67% voted in favour in the second round, or if >50% voted in the third round. The Oxford Centre for Evidence-Based Medicine levels of evidence derived from the SLR were added to each recommendation (Table 2). Finally, each task force member anonymously indicated the level of agreement (LoA) via online survey using a numeric rating scale, ranging from 0 (do not agree) to 10 (fully agree). The mean and SD of the LoA and the percentage of task force members with an agreement level ≥ 8 were recorded.

An agenda for future research was also formulated based on gaps in the evidence and contentious or controversial issues arising during the discussion.

Results

General Aspects

These recommendations and considerations are intended to advise healthcare professionals involved in the referral, acquisition or interpretation of MRI in patients with suspected axSpA. The targeted users of these recommendations are radiologists, rheumatologists, radiographers, primary care physicians and specialists in general medicine. The target population is patients with suspected or known axSpA. The recommendations may also inform patients participating in shared decision making, and healthcare providers involved in the coordination of care for patients with axSpA.

They are not intended as a complete document on the use of MRI in axSpA and should be interpreted depending on local circumstances and on the clinical context. Two overarching principles and seven recommendations have been proposed by the task force following a meeting of data presentation and a consensus exercise. These are shown in Table 3 and are discussed in detail below. This exercise also highlighted an agenda for future research, summarised in Table 4.

Overarching Principles

Two overarching principles were formulated – these were intended to be general and to provide background for the subsequent specific recommendations.

OP1: The diagnosis of axSpA is based on clinical, laboratory and imaging features.

This principle highlights the fact that imaging cannot be viewed in isolation and needs to be interpreted in the context of clinical presentation and results of laboratory investigations. The task force members highlighted that the sensitivity and specificity of MRI for the diagnosis of axSpA is likely to vary depending on the clinical setting in which patients are referred for the test and on the level of suspicion required to initiate a referral. MRI findings must therefore be combined with clinical and laboratory features to arrive at an overall diagnosis, and imaging features alone should not be regarded as diagnostic for axSpA.

OP2: Some patients with axSpA can have isolated inflammation of either the SIJs or spine.
Although the available evidence regarding the prevalence of spinal inflammation without SIJ inflammation is mixed (11–15), some studies report that spinal and SIJ inflammation can exist independently (13–15). The prevalence of spinal inflammation may depend on the clinical setting and on the type of cohort being studied. For example, patients enrolled in trials of therapeutic agents may have different features, including more severe disease, than those recruited in other cohorts. This overarching principle underpins recommendation 1, which is detailed below.

Recommendations

A total of seven recommendations have been formulated, which are summarised in Table 3 with corresponding levels of evidence and agreement.

Recommendation 1: When requesting an MRI for suspected axSpA, imaging of both the SIJs and the spine is recommended.

Since spinal inflammation can exist independently of SIJ inflammation in some patients (OP2), omitting the spine from MRI protocols increases the chances of 'missing' evidence of axial inflammation. Even in the absence of spinal inflammation, spinal MRI can be clinically useful in patients presenting with chronic back pain and has practical implications for their ongoing management. This recommendation conflicts with the 2015 EULAR recommendation proposing that MRI of the spine is not generally recommended to diagnose axial SpA (9), but is consistent with the latest National Institute of Clinical Excellence (NICE) guidance (2018) (16).

There are little data on how much of the spine should be imaged, since studies to date have varied substantially in terms of anatomical coverage. A commonly-used approach is to

image the thoracolumbar spine, but there is currently no evidence to support this choice compared to more complete (whole spine or whole body) or more limited (lumbar spine only) spine acquisition schemes. These recommendations have therefore deliberately omitted a precise recommendation regarding anatomical coverage, allowing scope for discretion depending on local resources and clinical setting.

Recommendation 2: T1-weighted and fat-suppressed, fluid sensitive sequences (including STIR, fat-saturated T2 or Dixon methods) are recommended for suspected axSpA.

The majority of studies investigating the use of MRI in the diagnosis of axSpA have used fat-suppressed, fluid sensitive sequences for the detection of bone marrow oedema, and T1-weighted sequences for the detection of structural changes including fat infiltration, erosions and ankylosis. However, there are very few studies which have compared the diagnostic utility of different sequences. Fat-saturated T2-weighted (FS-T2W) sequences provides similar information to the widely-used short inversion time inversion recovery (STIR) sequence (17), and may offer improvements in diagnostic sensitivity (18). However, task force members felt that further evidence was required to definitely demonstrate superiority of the FS-T2W sequence compared to STIR. Similarly, T2-weighted Dixon imaging may demonstrate improvement in contrast-to-noise ratio, but the sensitivity and specificity of imaging using this sequence has not been directly compared with STIR or FS-T2W imaging (19). It was highlighted that Dixon imaging can be a useful alternative in situations where conventional fat suppression is problematic, for example when imaging is performed close to metallic implants.

In the SIJs, the information provided by gadolinium-enhanced MRI is thought to largely overlap with that provided by fluid-sensitive sequences (20–22). Gadolinium-enhanced MRI of the SIJs should therefore be considered a non-essential part of MRI protocols for axSpA in the SIJs. However, there is little evidence on the value of gadolinium-enhanced imaging in the spine, which could provide additional information on facet joint inflammation or spinal enthesitis.

Recommendation 3: The minimum protocol when requesting an MRI for suspected axSpA should include sagittal images of the spine with extended lateral coverage and images of the SIJs which are at an oblique coronal plane to the joint.

This recommendation was based on expert opinion and current clinical practice, taking into account the required area to detect sacroiliitis and axial inflammation, whilst limiting study time and cost. Lateral coverage includes full coverage of the verterbrae up to and including the costovertebral and costotransverse joints. There have not been any specific studies addressing the optimal anatomical coverage for MRI in axSpA.

Recommendation 4: In the SIJs, the presence of bone marrow oedema, fatty infiltration or erosion is suggestive of the diagnosis of axSpA. The presence of more than one of these features increases the diagnostic confidence of axSpA.

Bone marrow oedema or osteitis (BMO) is thought to reflect an increase in free water content and vascularity in the bone marrow and can be detected as areas of increased signal intensity on fluid-sensitive sequences (particularly fat-suppressed, T2-weighted sequences) as discussed under Rec 2. The existing evidence suggests that bone marrow oedema is the most sensitive individual lesion for the diagnosis of axial SpA (15,23–27). However, using BMO as a solitary diagnostic criterion can lead to false positives. Specificity can be improved by considering BMO in combination with either erosions or fat infiltration (23–25,27). Again, we emphasise the importance of interpreting these lesions in the context of clinical and biochemical features (OP 1), in patients who are clinically suspected of having axSpA.

Fat infiltration is typically identified as an area of increased signal on T1-weighted images. Fat infiltration alone shows moderate sensitivity and specificity in the diagnosis of axSpA, but has a greater utility in AS and more established disease (23,24,28,29). Fat infiltration is thought to be more specific for the diagnosis of AS than for nr-axSpA, which may reflect its formation as a post-inflammatory chronic lesion (29). Similarly, periarticular erosions, which are visualised as low T1-signal bone defects at joint margin, demonstrate poor to moderate sensitivity, although some studies have shown relatively high specificity (24–26,28,29). Erosions are more sensitive in AS than in non-radiographic axial SpA or clinically-diagnosed SpA (28,29), and are more sensitive against a pre-specified MRI reference standard than against a clinical reference standard (24).

Vacuum phenomenon, sclerosis, enthesitis, and capsulitis can also be found in axSpA but have poor diagnostic performance in isolation (23,30)

There is some evidence that lesion-based diagnostic criteria, which use thresholds for the number of lesions required to suggest a diagnosis, can improve diagnostic performance (25). However, taskforce members did not feel that there was sufficient evidence to provide clear, useful lesion-based criteria for clinical use.

Recommendation 5: In the spine, the presence of multiple corner inflammatory lesions and/or multiple corner fatty lesions increases the diagnostic confidence of axSpA.

Active inflammatory lesions in the vertebral bodies are defined as increased signal on T2W or STIR sequences at the vertebral corners and adjacent to the vertebral end plates. These corner inflammatory lesions (previously described as Romanus lesions) demonstrate moderate sensitivity and specificity in the diagnosis of axSpA (28,31–34), whilst spinal fatty lesions have poor sensitivity and specificity for the diagnosis of axSpA (28,31–33). There remains uncertainty about how features on MRI spine should be integrated with those in the SIJ to optimise diagnostic performance in axSpA, but panel members felt that these lesions could form a useful part of the investigation and could increase diagnostic confidence.

Finally, degenerative changes in the spine are prevalent both in patients with axSpA and in the general population and these changes can become relevant when they mimic axSpA. Care should be taken to avoid the wrongfully recognition of inflammation and/or fatty lesions due to degeneration as axSpA lesions.

Recommendation 6: In the SIJs and/or spine the presence of characteristic new bone formation increases the diagnostic confidence of axSpA.

This recommendation is based on the available evidence and on expert opinion. Ankylosis of the sacroiliac joint is relatively insensitive for the diagnosis of axSpA, but demonstrates good specificity (23). Similarly, the presence of new bone formation/fat deposition in the joint space (which is referred to as backfill by some authors and typically manifests as increase in T1W signal in the joint space), demonstrates good specificity (30,35). The task force recommend that these features should increase diagnostic confidence where they are clear-cut or definite, although it is important to highlight that early ankylosis can be difficult and

may often be erroneously identified in healthy patients. Importantly, new bone formation can also arise in conditions related to axSpA, such as diffuse idiopathic skeletal hyperostosis (DISH), and care should be taken to avoid incorrect diagnosis in this situation.

Finally, the task force do not recommend the use of the term 'backfill'; instead the increase in T1W signal in the joint space is thought to represent marrow fat from bone formation in the joint (i.e. early stage of ankylosis) and should be referred to as such.

Recommendation 7: The full range and combination of active and structural lesions of the SIJs and spine should be taken into account when deciding if the MRI scan is suggestive of axSpA or not.

This recommendation is based on expert opinion and reflects an overall view of the available evidence. The panel suggests that both active and structural lesions, in both the SIJs and spine, should be used to arrive at an overall diagnostic probability. The importance of individual lesions should be considered according to Recommendations 4, 5 and 6, bearing in mind the increasing data on corresponding findings in patients with non-specific back pain (36) postpartum women (36) runners (36), soldiers (37) athletes (38) and the general population (39). There is currently insufficient evidence to recommend a specific scheme for 'weighting' lesions in different anatomical locations, or according to depth or intensity, and this will be a topic of further research. Lesion description of the SIJ and spine have been published by ASAS (40,41). However, these definitions are currently being updated by ASAS as part of large international MRI reading exercise (42). In summary, contextual interpretation of active and structural lesions is key to enhance diagnostic utility of MRI is patients with suspected axSpA.

Discussion

The diagnostic utility of MRI in axSpA is widely accepted. However, there is substantial heterogeneity in its acquisition and interpretation in suspected axial disease (5). This document provides specific recommendations addressing these areas with the aim of promoting an informed and consistent approach to MRI use in axSpA. Importantly, the recommendations were derived using a task force comprising equal numbers of rheumatologists and radiologists, thereby providing a balanced appraisal of the evidence

from both perspectives. Furthermore, all of the final recommendations received high levels of agreement, indicating a strong consensus between the two groups.

Previous EULAR recommendations regarding the use of imaging in spondyloarthritis did include detailed recommendations regarding MRI, but were much broader in their scope (9). By undertaking a focused review of the literature relating to the use of MRI, we were able to formulate specific recommendations regarding the use of MRI in the diagnostic pathway.

We have provided recommendations regarding lesions, anatomical coverage, and acquisition parameters. To our knowledge, this is the first exercise to consider the technical aspects of MRI in detail. However, it should be noted that there are currently few studies comparing different MRI techniques in terms of diagnostic performance, so the recommendations largely reflect the most prevalent – rather than necessarily the most effective - approaches to acquisition in the literature. Additionally, many emerging MRI techniques are at an early developmental stage and, due to study design considerations, did not meet the inclusion criteria for this review. We anticipate that these techniques will begin to reach maturity in the coming years and that more evidence regarding the diagnostic utility of these methods will emerge.

There are some limitations of the studies included in the SLR which should be highlighted, as they impact the confidence with which diagnostic performance statistics can be interpreted. For example, several of the included studies used a reference standard which included imaging, thus the reasoning of these studies is arguably somewhat circular. Even in studies which did not explicitly use imaging criteria in their reference standard, it is unclear whether patients were referred as a result of positive findings on MRI scans. There is a need to improve the reference standard for future studies, but precisely how to achieve this is unclear. One approach might be to use an 'enhanced' reference standard consisting of follow up to ensure that patients have 'definite' axSpA, although this would be difficult to achieve and expensive. In practice, the questions of diagnosis and prognosis are closely intertwined, since patients with more severe features can be diagnosed with greater confidence than those with subtle disease manifestations. Issues around prediction of outcome/severity in axSpA have been considered in the previous EULAR review by Mandl et al (9), and are also likely be a topic of future research.

This work has highlighted a number of potential avenues for future research, which have been summarised in Table 4. There is a lack of studies investigating the diagnostic utility of gadolinium-based contrast in the spine, and further research in this area would be informative. Similarly, there is little evidence investigating the utility of additional pelvic imaging in the diagnosis of axSpA. Although there is good evidence that imaging the spine is useful, the precise anatomical coverage which should be used is unclear, and studies specifically investigating this question are needed. Task force members also highlighted that quantitative MRI techniques, which can provide quantitative imaging biomarker measurements, might help to diagnose axSpA in the future. Similarly, new image analysis methods using techniques such as machine learning could be used to achieve intelligent diagnosis and to therefore improve the consistency of image interpretation. It was suggested that MRI reports might use a standard lexicon, for example using terms such as 'positive', 'indeterminate; and 'negative' to describe different levels of diagnostic certainty; this might offer an improvement to the current situation where the language used in radiological reports is variable and dependent on the reader's interpretation. Finally, the need to better be able to differentiate which MRI lesions are stress or biomechanically-induced, degenerative, infectious, and/or non-specific versus specific for axSpA, was also highlighted.

To conclude, a UK joint rheumatology and radiology consensus on the acquisition and interpretation of MRI in the investigation of axSpA was achieved. The recommendations are intended to standardise practice around the use of MRI and to enable a more informed, consistent approach to the diagnosis of axSpA.

Key messages

- A joint rheumatology and radiology consensus on the acquisition and the interpretation of MRI in axSpA was achieved.
- This consensus should help standardise practice around MRI and ensure a more informed, consistent approach to the diagnosis of axSpA.

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Competing interests

HMO has received grants and/or honoraria from Abbvie, Celgene, Eli-Lilly, Janssen, MSD, Novartis, Pfizer and UCB. PGC has performed consultancies or speakers bureaus for Abbvie, BMS, Novartis, Pfizer and Roche. PMM has received consulting/speaker's fees from Abbvie, BMS, Celgene, Janssen, MSD, Novartis, Pfizer, Roche and UCB. None of the other authors declared competing interests.

Tables and Figures

Table 1: Research questions (RQ) generated by the BRITSpA working group

RQ1	Which lesion, or combination of lesions, is most sensitive and specific for the diagnosis of axSpA?
RQ2	How does the choice of anatomical region influence diagnostic performance?
RQ3	How do MRI acquisition parameters influence diagnostic performance?

Table 2: Oxford Centre for Evidence Based Medicine 2011 levels of evidence for diagnostic studies

Level	**Definition**
1	Evidence from a systematic review of cross sectional studies with consistently applied reference standing and blinding
2	Individual cross-sectional studies with consistently applied reference standard and blinding
3	Non-consecutive studies or studies without consistently applied reference standard
4	Case controlled studies or poor or non-independent reference standard
5	Mechanism based reasoning

Table 3: Recommendations with levels of evidence (LoE) and level of agreement (LoA) . Numbers in column 'LoA' indicate the mean, SD (in parenthesis) and the percentage of task force members giving an agreement level ≥8. Note that the overarching principles are general statements and have therefore not been assigned with LoE.

Overarching principles (OP) and recommendations (Rec)		***LoE***	**LoA**
OP1	The diagnosis of axSpA is based on clinical, laboratory and imaging features.	-	9.7 (0.7) 100% ≥8
OP2	Some patients with axSpA can have isolated inflammation of either the SIJs or spine.	-	9.8 (0.4) 100% ≥8
Rec1	When requesting an MRI for suspected axSpA, imaging of both the SIJs and the spine is recommended.	3	9.1 (1.4) 88% ≥8
Rec2	T1-weighted and fat-suppressed, fluid sensitive sequences (including STIR[*], fat-saturated[ł] T2 or Dixon methods[‡]) are recommended for suspected axSpA.	2[*]/3[ł]/5[‡]	9.5 (0.8) 100% ≥8
Rec3	The minimum protocol when requesting an MRI for suspected axSpA should include sagittal images of the spine with extended lateral coverage and images of the SIJs which are at an oblique coronal plane to the joint.	5	8.8 (1.7) 88% ≥8
Rec4	In the SIJs, the presence of bone marrow oedema, fatty infiltration or erosion is suggestive of the diagnosis of axSpA. The presence of more than one of these features increases the diagnostic confidence of axSpA.	2	9.2 (1.2) 82% ≥8
Rec5	In the spine, the presence of multiple corner inflammatory lesions and/or multiple corner fatty lesions increases the diagnostic confidence of axSpA.	2	9.2 (0.8) 100% ≥8
Rec6	In the SIJs and/or spine the presence of characteristic new bone formation increases the diagnostic confidence of axSpA.	2	8.8 (1.1) 94% ≥8
Rec7	The full range and combination of active and structural lesions of the SIJs and spine should be taken into account when deciding if the MRI scan is suggestive of axSpA or not.	5	9.5 (0.6) 100% ≥8

Table 4: Future research agenda (RA) .

RA1	To define an improved reference standard for the diagnosis of axSpA, which can be used in future diagnostic performance studies in axSpA, and is ideally entirely independent of imaging. This could involve long-term follow up to ensure that all cases diagnosed have a true diagnosis of axSpA.
RA2	To investigate the diagnostic utility of gadolinium-based contrast in the spine.
RA3	To investigate the utility of additional pelvic imaging in the diagnosis of axial SpA.
RA4	To further investigate the utility of whole body-MRI for the diagnosis of axSpA, and to compare this with more limited acquisition protocols to determine the 'optimal' anatomical coverage.
RA4	To further investigate whether quantitative MRI methods can improve the sensitivity, specificity and reproducibility of diagnosis of axSpA.
RA5	To further investigate whether novel image analysis methods such as machine learning can improve the sensitivity, specificity and reproducibility of diagnosis of axSpA.
RA6	To investigate whether MRI reports can be produced using a standard lexicon, which simplifies interpretation for the referrer. This might include standardised descriptions of diagnostic certainty using terms such as 'positive', 'indeterminate' and 'negative'.
RA7	To better define and being able to differentiate which MRI lesions are stress or biomechanically-induced, degenerative, infectious, and/or non-specific versus specific for axSpA.

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