ARP Rheumatology 2024;3:254-257
https://doi.org/10.63032/SKWB5258

EDITORIAL

MRI in axial spondyloarthritis: redefining diagnostic and assessment paradigms

Weddell J[1, 2], Marzo-Ortega H[1, 2], Machado PM[3, 4, 5]

Background

Axial spondyloarthritis (axSpA) is a chronic immune-mediated condition characterised by inflammation in the axial skeleton entheses, leading to pain, stiffness, and, in some cases spinal fusion[1] Symptoms typically develop between the second and fourth decades of life. However, delays in diagnosis are common, with a mean of 6.7 years from symptom onset to diagnosis[2]. This delay is largely due to the absence of specific biomarkers and reliance on clinical symptoms, many of which are common and shared with other conditions, such as chronic back pain[3].

Historically, the clinical diagnosis of axSpA was supported by radiographic evidence of structural changes, including erosions, sclerosis or ankylosis in the sacroiliac joints (SIJs), or bridging syndesmophytes arising from spinal entheses. These structural changes are associated with reduced physical mobility and function, causing significant disability for patients[4, 5]. Advancements in MRI technology in the early 2000s enabled diagnosis before the development of structural changes in the SIJs or spine, allowing for the identification of an additional group of patients without detectable radiographic structural changes[6-8].

Consequently, the improved detection capabilities of MRI led to changes in disease definition and nomenclature. Patients with structural changes indicative of sacroiliitis visible on radiographs are classified as having radiographic axSpA (r-axSpA), formerly known as ankylosing spondylitis (AS). In contrast, those without radiographic changes are classified as having non-radiographic axSpA (nr-axSpA)[9]. This article summarises the role of MRI in axSpA (Figure 1).

[1] NIHR Leeds Biomedical Research Centre, Leeds Teaching Hospitals Trust, Leeds, UK.
[2] Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, Leeds, UK.
[3] Department of Neuromuscular Diseases & Centre for Rheumatology, University College London, London, UK
[4] NIHR University College London Hospitals Biomedical Research Centre, University College London Hospitals NHS Foundation Trust, London, UK
[5] Department of Rheumatology, Northwick Park Hospital, London North West University Healthcare NHS Trust, London, UK

Correspondence to: Pedro Machado
E-mail: p.machado@ucl.ac.uk

MRI as a diagnostic tool

Axial spondyloarthritis remains a clinical diagnosis; however, UK[10] and European guidelines[11] recommend the use of MRI in the diagnostic process, due to its ability to identify active inflammation in the spine and SIJs. Lesions suggestive of active inflammation include bone marrow oedema (BMO), defined as hyperintensities within the subcortical bone in images generated using T2-weighted sequences with a fat saturation module, such as Short Tau Inversion Recovery (STIR) or Spectral Attenuated Inversion Recovery (SPAIR) sequences. Other inflammatory lesions include capsulitis and enthesitis[12-14]. Lesions indicative of chronic structural changes, such as erosions, sclerosis, fat deposition/metaplasia, bone buds, and ankylosis, are visible on T1-weighted sequences and are thought to represent post-inflammatory bone changes[12-14]. Importantly, active and chronic lesions are non-specific to axSpA and can occur as a result of significant biomechanical stress, such as in postpartum women, athletes, and military personnel[12, 15]. Furthermore, up to 20% of individuals with axSpA have normal MRI findings. Therefore, any abnormal MRI findings (or their absence) must be interpreted in the context of the patient's symptoms and history.

A recent study from the Assessment in Spondyloarthritis international Society (ASAS) identified cut offs for active and structural lesions in the SIJs with a positive predictive value for axSpA greater than 95% for both active and chronic MRI lesions[16]. However, the prevalence of these changes in patients with a diagnosis of axSpA remains unclear[3, 12].

Regarding image acquisition, the most recent British Society for Spondyloarthritis (BRITSpA)[17] and ASAS/Spondyloarthritis Research And Treatment Network (SPARTAN)[18] guidelines recommend performing MRI of the whole spine and SIJ using a T1-weighted sequence to identify chronic inflammatory lesions, and a fat-suppressed T2-weighted sequence, most commonly STIR, to identify active inflammatory lesions. The ASAS/SPARTAN guidelines also suggest using a cartilage-sensitive sequence, such as the Volumetric Interpolated Breath-Hold Examination (VIBE) sequence, to better detect erosions at the SIJ level.

MRI as a prognostic tool

In addition to its utility in diagnosing axSpA, MRI provides valuable prognostic information. Numerous studies have shown that patients with objective evidence

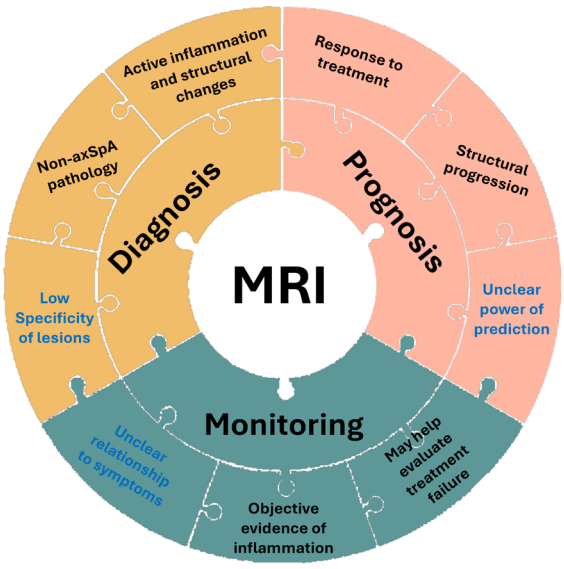

Figure 1. The role of MRI in axial spondyloarthritis

of active inflammation, such as BMO or elevated CRP, are more likely to respond to biological/target synthetic disease-modifying antirheumatic drug (b/ts DMARD) therapy than those without such findings[19]. Inflammatory MRI lesions, such as BMO, also predict the location and development of structural changes at the SIJ[20] and spine level[21].

MRI as a monitoring tool

The role of MRI in monitoring disease activity in axSpA remains unclear. The most recent ASAS/EULAR guidelines[22] do not recommend routine use of MRI for this purpose due to evidential uncertainties and cost implications, instead advising clinicians to make decisions on a case-by-case basis. Despite this, MRI appears to be commonly used for assessing disease activity in clinical practice. A recent UK survey of rheumatologists found that 10.3% used MRI routinely and 36.9% used it frequently for this purpose[23]. Similarly, a clinical audit at the Leeds Teaching Hospitals NHS Trust, UK, revealed that one in six MRIs performed in this tertiary centre were for disease monitoring. Among these, half showed inflammation, and clinicians were three times more likely to switch treatment in patients with MRI-detected inflammation[24], underscoring the importance of MRI in guiding clinical decision-making.

The relationship between MRI-detected inflammation and clinical outcomes in axSpA remains unclear, with conflicting evidence. Real-world data from the DESIR cohort of patients with newly diagnosed axSpA showed an association between changes in MRI SIJ[25] and MRI spine[26] scores and improvement in Axial Spondyloarthritis Disease Activity Score (ASDAS) between baseline and two years in males, but not in females. However, a cross-sectional study in the UK found no relationship between Spondyloarthritis Research Consortium of Canada (SPARCC) scores and high or low disease activity as defined by ASDAS or Bath Ankylosing Spondylitis Disease Activity Index (BASDAI)[27]. Concordance between clinical remission and absence of MRI inflammation was also shown to be limited in the clinical trial setting[28].

In a subgroup of patients reporting subjective loss of response at the end of their TNFi treatment cycle, the temporal association between subjective loss of response and a corresponding increase in BMO suggests a causal relationship. Overall, 57.9% of these patients had BMO lesions at the end of their treatment cycle. On repeat MRI four days into the subsequent treatment cycle, the number of MRI lesions decreased, and clinical outcome measures improved, further suggesting a relationship between increases in BMO and clinical loss of response to TNFi therapy[29].

Similarly, the relationship between MRI findings and serum inflammatory markers is complex, with evidence suggesting an association between MRI changes in the spine and CRP levels, but not in the SIJs[30, 31].

Limitations and future perspectives

Despite the widespread use of MRI in axSpA, several limitations must be considered. MRI interpretation relies on qualitative assessments by trained professionals, with few objective and quantifiable parameters. Semi-quantitative scoring systems, along with standardised MRI requesting[32] and reporting[33] guidelines, have been developed to enhance objectivity; however, significant variations in interobserver agreement persist among different readers. Additionally, MRI signals are non-specific to disease processes and are often derived from tissue with multiple overlapping properties, such as co-existing active and chronic changes.

In recent years, technical advancements have driven the development of quantitative MRI techniques. These methods leverage small adjustments in MRI acquisition parameters to generate objective numerical data on various tissue properties, such as T2 relaxation time, fat fraction, or diffusivity[34-36]. Such techniques can differentiate between overlapping disease processes, such as fat deposition/metaplasia and active inflammation, and provide objective, quantifiable parameters for monitoring disease activity. Alongside improvements in MRI acquisition, recent advancements in artificial intelligence (AI) hold promise for the objective identification and quantification of inflammatory lesions, streamlined MRI reporting, and enhanced diagnosis and monitoring of axSpA.

Conclusions

MRI has revolutionised the management of axial spondyloarthritis, fundamentally transforming our approach to this disease. It is now integral to the diagnostic process and provides clinicians with valuable prognostic

information. However, MRI has several limitations, and any findings must be interpreted in the context of the patient's symptoms and history. Future research should focus on quantitative approaches to enhance detection, diagnosis, and objectivity in MRI, as well as exploring its potential as a monitoring tool to improve care and outcomes in axSpA.

Acknowledgements

HM-O is supported by the National Institute for Health Research (NIHR) Leeds Biomedical Research Centre (LBRC), Leeds Teaching Hospitals Trust. PMM is supported by the NIHR University College London Hospitals Biomedical Research Centre, University College London Hospitals NHS Foundation Trust. The views expressed are those of the authors and not necessarily those of the (UK) National Health Service (NHS), the NIHR, or the (UK) Department of Health.

Conflicts of interest

PMM has received honoraria from Abbvie, BMS, Celgene, Eli Lilly, Galapagos/Alfasigma, Janssen, MSD, Novartis, Orphazyme, Pfizer, Roche and UCB. No conflicts declared by the other authors.

REFERENCES

1. Navarro-Compan V, Sepriano A, El-Zorkany B, van der Heijde D. Axial spondyloarthritis. Ann Rheum Dis. 2021 Dec; 80(12):1511-1521. https://doi.org/10.1136/annrheumdis-2021-221035
2. Zhao SS, Pittam B, Harrison NL, Ahmed AE, Goodson NJ, Hughes DM. Diagnostic delay in axial spondyloarthritis: a systematic review and meta-analysis. Rheumatology (Oxford). 2021 Apr 6; 60(4):1620-1628. https://doi.org/10.1093/rheumatology/keaa807
3. Carvalho PD, Machado PM. How to investigate: Early axial spondyloarthritis. Best Pract Res Clin Rheumatol. 2019 Aug; 33(4):101427. https://doi.org/10.1016/j.berh.2019.07.001
4. Machado P, Landewe R, Braun J, Hermann KG, Baker D, van der Heijde D. Both structural damage and inflammation of the spine contribute to impairment of spinal mobility in patients with ankylosing spondylitis. Ann Rheum Dis. 2010 Aug; 69(8):1465-1470. https://doi.org/10.1136/ard.2009.124206
5. Machado P, Landewe R, Braun J, Hermann KG, Baraliakos X, Baker D, et al. A stratified model for health outcomes in ankylosing spondylitis. Ann Rheum Dis. 2011 Oct; 70(10):1758-1764. https://doi.org/10.1136/ard.2011.150037
6. Hayward RJ, Machado PM. Classification Criteria in Axial Spondyloarthritis: What Have We Learned; Where Are We Going? Rheum Dis Clin North Am. 2020 May; 46(2):259-274. https://doi.org/10.1016/j.rdc.2020.01.008
7. Rudwaleit M, Landewe R, van der Heijde D, Listing J, Brandt J, Braun J, et al. The development of Assessment of SpondyloArthritis international Society classification criteria for axial spondyloarthritis (part I): classification of paper patients by expert opinion including uncertainty appraisal. Ann Rheum Dis. 2009 Jun; 68(6):770-776. https://doi.org/10.1136/ard.2009.108217
8. Rudwaleit M, van der Heijde D, Landewe R, Listing J, Akkoc N, Brandt J, et al. The development of Assessment of SpondyloArthritis international Society classification criteria for axial spondyloarthritis (part II): validation and final selection. Ann Rheum Dis. 2009 Jun; 68(6):777-783. https://doi.org/10.1136/ard.2009.108233
9. van der Heijde D, Molto A, Ramiro S, Braun J, Dougados M, van Gaalen FA, et al. Goodbye to the term 'ankylosing spondylitis', hello 'axial spondyloarthritis': time to embrace the ASAS-defined nomenclature. Ann Rheum Dis. 2024 Apr 11; 83(5):547-549. https://doi.org/10.1136/ard-2023-225185
10. National Institute for Health and Care Excellence, NICE. Spondyloarthritis in over 16s: diagnosis and management [NG65] [Internet]. 2017 Jun. Available from: https://www.nice.org.uk/guidance/ng65.
11. Mandl P, Navarro-Compan V, Terslev L, Aegerter P, van der Heijde D, D'Agostino MA, et al. EULAR recommendations for the use of imaging in the diagnosis and management of spondyloarthritis in clinical practice. Ann Rheum Dis. 2015 Jul; 74(7):1327-1339. https://doi.org/10.1136/annrheumdis-2014-206971
12. Caetano AP, Mascarenhas VV, Machado PM. Axial Spondyloarthritis: Mimics and Pitfalls of Imaging Assessment. Front Med (Lausanne). 2021; 8:658538. https://doi.org/10.3389/fmed.2021.658538
13. Maksymowych WP, Lambert RG, Ostergaard M, Pedersen SJ, Machado PM, Weber U, et al. MRI lesions in the sacroiliac joints of patients with spondyloarthritis: an update of definitions and validation by the ASAS MRI working group. Ann Rheum Dis. 2019 Nov; 78(11):1550-1558. https://doi.org/10.1136/annrheumdis-2019-215589
14. Baraliakos X, Ostergaard M, Lambert RG, Eshed I, Machado PM, Pedersen SJ, et al. MRI lesions of the spine in patients with axial spondyloarthritis: an update of lesion definitions and validation by the ASAS MRI working group. Ann Rheum Dis. 2022 Aug 11; 81(9):1243-1251. https://doi.org/10.1136/annrheumdis-2021-222081
15. Baraliakos X, Richter A, Feldmann D, Ott A, Buelow R, Schmidt CO, et al. Frequency of MRI changes suggestive of axial spondyloarthritis in the axial skeleton in a large population-based cohort of individuals aged <45 years. Ann Rheum Dis. 2020 Feb; 79(2):186-192. https://doi.org/10.1136/annrheumdis-2019-215553
16. Maksymowych WP, Lambert RG, Baraliakos X, Weber U, Machado PM, Pedersen SJ, et al. Data-driven definitions for active and structural MRI lesions in the sacroiliac joint in spondyloarthritis and their predictive utility. Rheumatology (Oxford). 2021 Oct 2; 60(10):4778- 4789. https://doi.org/10.1093/rheumatology/keab099
17. Bray TJP, Jones A, Bennett AN, Conaghan PG, Grainger A, Hodgson R, et al. Recommendations for acquisition and interpretation of MRI of the spine and sacroiliac joints in the diagnosis of axial spondyloarthritis in the UK. Rheumatology (Oxford). 2019 Oct 1; 58(10):1831-1838. https://doi.org/10.1093/rheumatology/kez173
18. Lambert RGW, Baraliakos X, Bernard SA, Carrino JA, Diekhoff T, Eshed I, et al. Development of international consensus on a standardised image acquisition protocol for diagnostic evaluation of the sacroiliac joints by MRI: an ASAS-SPARTAN collaboration. Ann Rheum Dis. 2024 Nov 14; 83(12):1628-1635. https://doi.org/10.1136/ard-2024-225882
19. Karmacharya P, Gupta S, Shahukhal R, Khanal R, Murad MH, Gensler LS. Effect of Biologics in Subgroups of Axial Spondyloarthritis Based on Magnetic Resonance Imaging and C-Reactive Protein: A Systematic Review and Meta-Analysis. ACR Open Rheumatol. 2023 Sep; 5(9):481-489. https://doi.org/10.1002/acr2.11581
20. Rodrigues-Manica S, Sepriano A, Ramiro S, Landewe R, Claudepierre P, Molto A, et al. Bone marrow edema in the sacroiliac joints is associated with the development of structural lesions at the same anatomical location over time in patients with axial spondyloarthritis. Semin Arthritis Rheum. 2023 Aug; 61:152225. https://doi.org/10.1016/j.semarthrit.2023.152225

21. Machado PM, Baraliakos X, van der Heijde D, Braun J, Landewe R. MRI vertebral corner inflammation followed by fat deposition is the strongest contributor to the development of new bone at the same vertebral corner: a multilevel longitudinal analysis in patients with ankylosing spondylitis. Ann Rheum Dis. 2016 Aug; 75(8):1486-1493. https://doi.org/10.1136/annrheumdis-2015-208011
22. Ramiro S, Nikiphorou E, Sepriano A, Ortolan A, Webers C, Baraliakos X, et al. ASAS-EULAR recommendations for the management of axial spondyloarthritis: 2022 update. Ann Rheum Dis. 2023 Jan; 82(1):19-34. https://doi.org/10.1136/ard-2022-223296
23. Weddell J, Bray TJP, Sengupta R, McGonagle D, Machado PM, Marzo-Ortega H. Current usage of and perspectives on the use of MRI to assess treatment non-response in axial spondyloarthritis: a UK-based survey. Rheumatol Adv Pract. 2024; 8(4):rkae139. https://doi.org/10.1093/rap/rkae139
24. Weddell J, Shah R, Rossi L, Robinson P, Barr A, Vandevelde C, et al. POS0521 Real World Evidence Shows That Repeat MRI Is of Utility in the Evaluation of Treatment Non-Response in Axial Spondyloarthritis- Data from a Tertiary Rheumatology Centre. Ann Rheum Dis. 2024 Jun; 1;83(Suppl 1):935-6. https://doi.org/10.1136/annrheumdis-2024-eular.5202
25. Navarro-Compan V, Ramiro S, Landewe R, Dougados M, Miceli-Richard C, Richette P, et al. Disease activity is longitudinally related to sacroiliac inflammation on MRI in male patients with axial spondyloarthritis: 2-years of the DESIR cohort. Ann Rheum Dis. 2016 May; 75(5):874-878. https://doi.org/10.1136/annrheumdis-2015-207786
26. Navarro-Compan V, Ramiro S, Landewe R, Dougados M, Miceli-Richard C, Richette P, et al. In patients with axial spondyloarthritis, inflammation on MRI of the spine is longitudinally related to disease activity only in men: 2 years of the axial spondyloarthritis DESIR cohort. Ann Rheum Dis. 2018 Mar; 77(3):470-472. https://doi.org/10.1136/annrheumdis-2016-210697
27. MacKay JW, Aboelmagd S, Gaffney JK. Correlation between clinical and MRI disease activity scores in axial spondyloarthritis. Clin Rheumatol. 2015 Sep; 34(9):1633-1638. https://doi.org/10.1007/s10067-015-2936-8
28. Braun J, Baraliakos X, Hermann KG, Landewe R, Machado PM, Maksymowych WP, et al. Effect of certolizumab pegol over 96 weeks of treatment on inflammation of the spine and sacroiliac joints, as measured by MRI, and the association between clinical and MRI outcomes in patients with axial spondyloarthritis. RMD Open. 2017; 3(1):e000430. https://doi.org/10.1136/rmdopen- 2017-000430
29. Harrison SR, Ansell R, Mathieson HR, Merashli M, Busquets-Perez N, McGonagle D, et al. Subjective loss of clinical response to TNFi in axSpA relates to recurrence of MRI bone marrow oedema particularly with long-acting agents. Rheumatology (Oxford). 2022 Apr 18; 61(SI):SI86- SI91. https://doi.org/10.1093/rheumatology/keab571
30. Machado P, Landewe RB, Braun J, Baraliakos X, Hermann KG, Hsu B, et al. MRI inflammation and its relation with measures of clinical disease activity and different treatment responses in patients with ankylosing spondylitis treated with a tumour necrosis factor inhibitor. Ann Rheum Dis. 2012 Dec; 71(12):2002-2005. https://doi.org/10.1136/annrheumdis-2012-201999
31. Tian H, Li T, Wang Y, Lu H, Lin L, Wu X, et al. The correlations between C-reactive protein and MRI-detected inflammation in patients with axial spondyloarthritis: a systematic review and meta- analysis. Clin Rheumatol. 2023 Sep; 42(9):2397-2407. https://doi.org/10.1007/s10067-023- 06658-w
32. Diekhoff T, Giraudo C, Machado PM, Mallinson M, Eshed I, Haibel H, et al. Clinical information on imaging referrals for suspected or known axial spondyloarthritis: recommendations from the Assessment of Spondyloarthritis International Society (ASAS). Ann Rheum Dis. 2024 Nov 14; 83(12):1636-1643. https://doi.org/10.1136/ard-2024-226280
33. Diekhoff T, Eshed I, Giraudo C, Haibel H, Hermann KGA, de Hooge M, et al. Reporting Sacroiliac Joint Imaging Performed for Known or Suspected Axial Spondyloarthritis: Assessment of SpondyloArthritis International Society Recommendations. Radiology. 2024 Jun; 311(3):e231786. https://doi.org/10.1148/radiol.231786
34. Laurent D, Riek J, Sinclair CDJ, Houston P, Roubenoff R, Papanicolaou DA, et al. Longitudinal Changes in MRI Muscle Morphometry and Composition in People With Inclusion Body Myositis. Neurology. 2022 Aug 30; 99(9):e865-e876. https://doi.org/10.1212/WNL.0000000000200776
35. Morrow JM, Sinclair CD, Fischmann A, Machado PM, Reilly MM, Yousry TA, et al. MRI biomarker assessment of neuromuscular disease progression: a prospective observational cohort study. Lancet Neurol. 2016 Jan; 15(1):65-77. https://doi.org/10.1016/S1474- 4422(15)00242-2
36. Thorley N, Jones A, Ciurtin C, Castelino M, Bainbridge A, Abbasi M, et al. Quantitative magnetic resonance imaging (qMRI) in axial spondyloarthritis. Br J Radiol. 2023 Mar 1; 96(1144):20220675. https://doi.org/10.1259/bjr.20220675