The role of sacro-iliac joint magnetic resonance imaging in the diagnosis of axial spondyloarthritis: focus on differential diagnosis in women

G. Besutti[1,2], C. Marvisi[3,4], F. Muratore[3,5], L. Spaggiari[1]

[1]*Radiology Unit, Azienda USL-IRCCS di Reggio Emilia, Italy;*
[2]*Department of Medical and Surgical Sciences, University of Modena and Reggio Emilia, Modena, Italy;*
[3]*Rheumatology Unit, Azienda USL-IRCCS di Reggio Emilia, Italy;*
[4]*Clinical and Experimental Medicine PhD Program, University of Modena and Reggio Emilia, Modena, Italy;*
[5]*University of Modena and Reggio Emilia, Modena, Italy*

SUMMARY

Objective. To review the role of sacro-iliac magnetic resonance imaging (MRI) in the diagnosis of axial spondyloarthritis (AxSpA), with a focus on gender differences.

Methods. The experience of the authors and the results of an informal literature review are reported.

Results. Inflammatory changes of the sacro-iliac joint are the hallmark of AxSpA. Early, non-radiographic sacroiliitis may be diagnosed with MRI through the assessment of bone marrow edema (BMO) as well as concomitant structural damage. The MRI protocol should include three necessary sequences, *i.e.,* fat-saturated T2-weighted sequences on two orthogonal planes, T1-weighted semi-coronal sequence, and fat-suppressed T1-weighted semi-coronal sequence. Inflammatory changes comprise required signs (BMO and/or osteitis) and additional signs, including synovitis (better defined as joint space enhancement), enthesitis, and capsulitis. Structural changes consist of erosions, sclerosis, fat metaplasia, and ankylosis. Due to mechanical axial strain, inflammatory changes in the sacro-iliac joint can be found in healthy individuals, runners, and patients with nonspecific low back pain. The prevalence of BMO is higher in women during pregnancy and postpartum, even 12 months after childbirth, but the extent and distribution of MRI findings may help in the differential diagnosis. Other challenges in the MRI diagnosis of sacroiliitis are subchondral T2 hyperintensity during developmental age, periarticular sclerosis in healthy subjects, or osteitis condensans ilii, and several pathological conditions that may mimic AxSpA, some of which are more frequently found in women.

Conclusions. The described diagnostic challenges impose a multidisciplinary approach combining imaging findings with clinical and laboratory data.

Key words: *Axial spondyloarthritis, sacro-iliac joint, sacroiliitis, magnetic resonance, women health.*

Reumatismo, 2024; 76 (3): 168-173

INTRODUCTION

Axial spondyloarthritis (AxSpA) is a chronic inflammatory disease that predominantly involves the axial skeleton, including the sacro-iliac joint (SIJ) and the spine. In particular, inflammatory changes of the SIJ are the hallmark of AxSpA (1).

In 2009, the Assessment in SpondyloArthritis International Society (ASAS) focused on the differentiation between radiographic and non-radiographic AxSpA (2). In fact, X-rays are the first imaging modality used in clinical practice, being easily available, not expensive, and highly diagnostic in cases of definite structural damage. However, in non-radiographic AxSpa, structural damage has not occurred yet. In this early disease, X-rays do not provide any diagnostic information. For this reason, magnetic resonance imaging (MRI) has been included in the diagnostic criteria of AxSpA, being able to identify inflammatory lesions that can be present when structural damage is not detectable (2). In 2016, the definition of a "positive MRI" was further specified by the ASAS MRI Working Group (3). In particular, evidence of bone

Corresponding author:
Giulia Besutti
Radiology Unit
Azienda USL-IRCCS di Reggio Emilia,
Reggio Emilia, Italy.
E-mail: giulia.besutti@ausl.re.it

marrow inflammation is always required for the definition of active sacroiliitis, but also MRI features of concomitant SIJ structural damage, especially erosions, or other signs of inflammation may contribute to the definite diagnosis.
The use of MRI in clinical practice has dramatically increased the number of non-radiographic AxSpA diagnoses. However, other inflammatory and non-inflammatory conditions may mimic the typical findings of sacroiliitis, with some of these conditions being particularly relevant in women of different ages. Thus, it is imperative to use a standardized MRI acquisition protocol, to correctly interpret imaging findings, and to decline such imaging findings in the correct clinical context, including demographic, clinical, and laboratory information (1, 4).

MAGNETIC RESONANCE IMAGING PROTOCOL

The recommended standard MRI protocol to be used to evaluate the presence of sacroiliitis in the suspect of AxSpA comprises three sequences, including sequences necessary to evaluate bone marrow edema (BMO) and sequences useful to evaluate structural damage (5, 6).
The presence of BMO should be assessed on fat-saturated T2-weighted sequences, usually short tau inversion recovery (STIR). Such sequences should be acquired on two orthogonal planes (semi-coronal and semi-axial planes) and are also useful for the assessment of inflammatory changes other than BMO.
Structural damage should be evaluated both on T1-weighted semi-coronal sequence, useful for assessment of sclerosis, fat deposition, and ankylosis, and on fat-suppressed T1-weighted semi-coronal sequence, which is cartilage-sensitive and better depicts the changes of articular surfaces, specifically erosions.
The three aforementioned sequences represent the recommended protocol. Other adjunctive sequences have been proposed, but there is no definite evidence that they provide added value for the diagnosis of active sacroiliitis (7, 8).
Particularly, the post-gadolinium fat-suppressed T1-weighted sequence is useful to identify increased vascularization in inflammatory lesions and to better assess the presence of capsulitis, synovitis, and enthesitis (4). Moreover, it has recently been suggested that the evaluation of post-gadolinium pathological enhancement (osteitis and synovitis) may be more sensitive than the evaluation of BMO alone in the assessment of response to tumor necrosis factor antagonist therapy (9).
The use of other sequences, such as diffusion-weighted imaging (DWI), its evolution intravoxel incoherent motion-DWI, as well as T1 or T2 mapping, is controversial and still limited to the research setting (4).

MAGNETIC RESONANCE IMAGING DIAGNOSTIC FEATURES OF ACTIVE SACROILIITIS

Among inflammatory changes, BMO (hyperintense in STIR and hypointense in T1-weighted images) and/or osteitis (increased enhancement in post-gadolinium fat-suppressed T1-weighted images) are the required signs to meet the diagnosis of active sacroiliitis (Figure 1) (3, 5). For this reason, these signs should be clearly present, typically located in the subchondral bone, and have a highly suggestive appearance (3). Moreover, the degree of STIR hyperintensity reflects the extent of the inflammatory activity.
Other inflammatory changes are neither required nor sufficient for the diagnosis of active sacroiliitis. They involve periarticular and intraarticular soft tissues, including synovitis affecting the synovial part of the SIJ, enthesitis involving the bone insertion of periarticular ligaments and tendons, and capsulitis of the joint capsule at the anterior and poster articular borders in axial slices (3, 5). Similarly to what is described for bone marrow, at these sites, MRI signs of inflammation include hyperintensity in STIR and post-gadolinium enhancement. Contrast administration is particularly useful for the assessment of synovitis because physiological joint fluid appears hyperintense in STIR images and can be mislead-

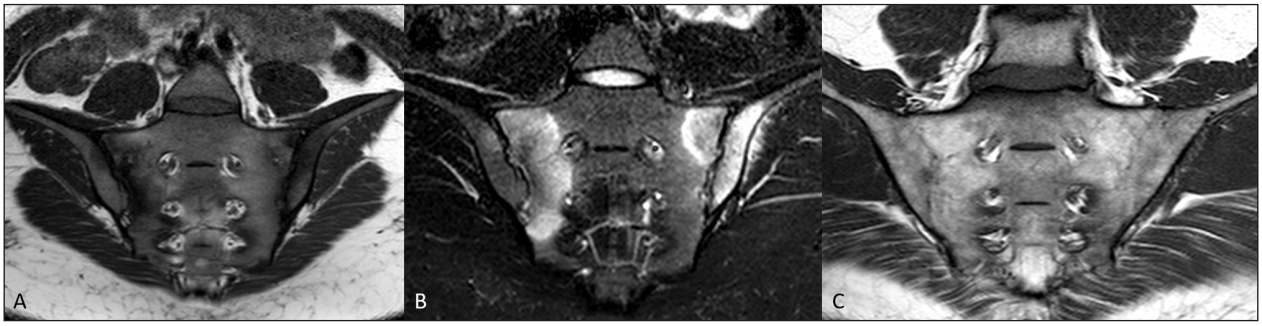

Figure 1 - Patients with axial spondyloarthritis. Active sacroiliitis with bone marrow edema visible as hypointense areas in semi-coronal T1-weighted images (A) and hyperintense areas in semi-coronal short tau inversion recovery images (B), with typical distribution and extensive depth in the periarticular bone. Long-term axial spondyloarthritis with definite structural damage visible as ankylosis with continuous bone marrow signal intensity of iliac and sacral bone, and absent joint cavity (C).

ing. Thus, in recent updates, the term synovitis has been replaced with "joint space enhancement" (10).

Among structural changes that can contribute to the diagnosis of active sacroiliitis, erosions are the most important (3, 5). Erosions are bony defects at the bone-cartilage interface, which can be hyperintense in STIR images if associated with active inflammation but are generally better assessed on fat-suppressed T1-weighted images. SIJ pseudo-widening may be the result of a confluence of many erosions. Sclerosis typically occurs in the subchondral bone, presenting as at least 5 mm-wide bands, hypointense in all sequences. Fat deposition or metaplasia, presenting as areas of T1 hyperintensity and hypointensity in STIR, is typically detected in periarticular bone marrow areas or inside erosions and is sharply defined from the normal bone marrow. It is also called "backfill" and probably represents an intermediate stage between erosion/inflammation and bone bridge formation towards ankylosis (11). Ankylosis occurs when the joint cavity cannot be outlined, the cortex on both articular sides tends to disappear, and the bone marrow signal intensity of the iliac bone and sacrum becomes a continuum (Figure 1) (10).

DIFFERENTIAL DIAGNOSIS: FOCUS ON WOMEN

The finding of BMO/osteitis should always be considered in the clinical context and in an objective way in order to assess if the MRI appearance is highly suggestive of active sacroiliitis, particularly for small solitary lesions (10). In fact, some degree of inflammation can be found in mechanical and degenerative conditions, as well as in post-traumatic, infectious, or neoplastic diseases.

Mechanical strain

In recent reports, low-grade BMO has been found in up to 25% of healthy individuals, runners, and patients with nonspecific low back pain, probably as a consequence of axial skeleton repetitive strain injuries (12-14).

Due to the slight differences in pelvic inclination and SIJ anatomy, women are more prone than men to develop MRI changes associated with mechanical axial strain. This is particularly true during pregnancy and in the *peripartum* and postpartum, when anatomical changes occur in the woman's pelvic walls. In fact, BMO has been described in more than 50% of women presenting with postpartum back pain (14, 15). In longitudinal studies, BMO was frequently found during and after pregnancy, also in asymptomatic women, peaking at three months postpartum but sometimes persisting also at 12 months postpartum (16, 17). Hence, the interpretation of SIJ MRI in this period of a woman's life could be particularly challenging. In sacroiliitis, BMO is usually more extensive, and the distribution of inflammatory lesions is diffuse, involv-

ing both the cartilaginous and the ligamentous portions of the joint. On the other hand, strain-related BMO in pregnancy and postpartum is predominantly located in the anterior and middle cartilaginous joint portions. Associated structural changes, including erosion, sclerosis, and fat lesions, are rare during pregnancy, but they tend to increase postpartum, suggesting the evolution of some inflammatory lesions to structural damage and making the differential diagnosis with AxSpA even more challenging (16, 17).

Developmental age

During childhood and adolescence, an increase in T2 and STIR signal intensity in the sacral bone marrow adjacent to SIJ should be expected and not be misdiagnosed as BMO (18). Since the conversion of cartilage into bone occurs in the subchondral regions of the SIJ, these regions present with increased vascularization in adolescence with respect to skeletal maturity (*i.e.*, 15 years in girls and 17 years in boys), resulting in the aforementioned T2 hyperintensity.

Physiological sclerosis and osteitis condensans ilii

Small areas of periarticular sclerosis can be found in healthy subjects and are more common above the age of 40, especially in obese subjects and multiparous women. Osteitis condensans ilii is a benign and usually incidentally found condition with a female predominance that has been associated with previous pregnancies (19). Although subchondral sclerosis, sometimes with subtle BMO at the periphery of the sclerotic region, may mimic AxSpA, the triangular shape, the distribution limited to the anterior portion of the SIJ, and the regular articular margins, without erosion, are usually helpful in the differential diagnosis.

Pathological conditions other than axial spondyloarthritis

Sacral stress fractures may occur after minor trauma or overuse in athletes, while sacral insufficiency fractures are common in elderly osteoporotic patients, more frequently women, or following pelvic radiotherapy, particularly for gynecological malignancies, mostly cervical cancer (20). Occasionally, stress fractures may occur in the postpartum (21). The MRI appearance of sacral insufficiency fracture includes frequently bilateral extensive BMO (hyperintensity in STIR and hypointensity in T1-weighted sequences), and T1-hypointense fracture lines commonly aligned vertically through the sacral ala (Figure 2). A horizontal line may co-exist through the sacral body, forming a typical H-shaped fracture. In osteoporotic elderly patients, concomitant insufficiency fractures can be found in the pubic bones near the symphysis. BMO distribution and concomitant fracture lines are the main clues for differential diagnosis with sacroiliitis.

In the case of septic sacroiliitis, inflammatory changes usually spread to soft tissue (including iliacus and gluteal muscles), sometimes developing fluid collection, while in AxSpA sacroiliitis, they remain limited to

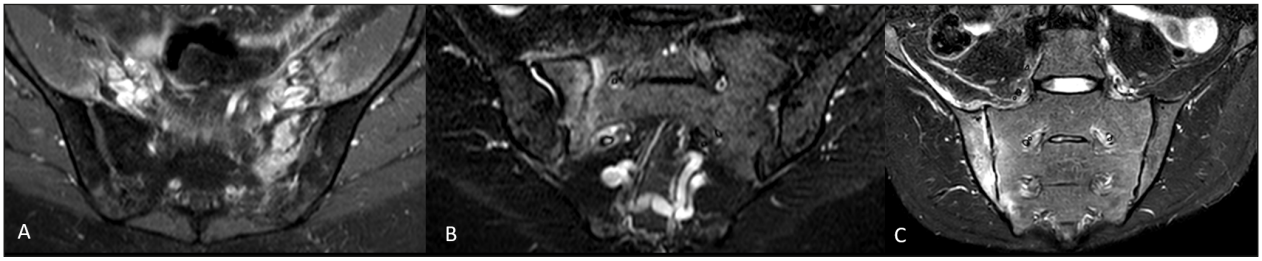

Figure 2 - A) Axial fat-saturated T1-weighted post-gadolinium sequence showing hyperenhancement with hypointense vertical line in a 56-year-old patient with insufficiency fracture of the left sacral ala 9 months after external beam radiotherapy for cervical cancer; B) semi-coronal short tau inversion recovery (STIR) sequence showing bone marrow edema and vertical fracture at the right sacral ala in a 32-weeks pregnant 31-year-old woman; C) semi-coronal STIR sequence in a 28-year-old female patient with right septic sacroiliitis: bone marrow edema is unilateral and concurrent soft tissue edema is visible behind the iliac muscle.

the bone and articular structures (Figure 2). Rarely, secondary inflammation can also be found in neoplastic diseases, but MRI appearance is usually very different from sacroiliitis. Osteoarthritis of SIJ, occurring usually in the elderly, may present with small subchondral BMO areas along the SIJ, predominantly on the iliac side, and slight subchondral sclerosis, but other signs co-exist, including marginal osteophytosis, joint space narrowing, and subchondral cysts.

CONCLUSIONS

MRI is highly sensitive for the diagnosis of sacroiliitis in early phases, but not highly specific. To avoid the risk of overdiagnosis and overtreatment, it is necessary to be aware that some AxSpA MRI findings may be found in other physiological and pathological conditions. In women, pregnancy and postpartum, as well as pathological conditions with female predominance, may introduce peculiar diagnostic challenges. A multidisciplinary assessment, considering imaging findings in the context of signs, symptoms, and laboratory data, is mandatory.

Contributions
GB, writing of the first draft. All the authors made a substantial intellectual contribution, read and approved the final version of the manuscript, and agreed to be accountable for all aspects of the work.

Conflict of interest
The authors have no conflicts of interest to declare.

Ethics approval and consent to participate
Bot applicable.

Patient consent for publication
Consent for publication was collected from patients whose images have been included in the study.

Funding
None.

Availability of data and materials
Not applicable.

REFERENCES

1. Navarro-Compán V, Sepriano A, El-Zorkany B, van der Heijde D. Axial spondyloarthritis. Ann Rheum Dis 2021; 80: 1511-21.
2. Rudwaleit M, Landewé 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; 68: 770-6.
3. Lambert RG, Bakker PA, van der Heijde D, Weber U, Rudwaleit M, Hermann KG, et al. Defining active sacroiliitis on MRI for classification of axial spondyloarthritis: update by the ASAS MRI working group. Ann Rheum Dis 2016; 75:1958-63.
4. de Hooge M, Diekhoff T, Poddubnyy D. Magnetic resonance imaging in spondyloarthritis: friend or foe?. Best Pract Res Clin Rheumatol 2023; 37:101874.
5. Rudwaleit M, Jurik AG, Hermann KG, Landewé R, van der Heijde D, Baraliakos X, et al. Defining active sacroiliitis on magnetic resonance imaging (MRI) for classification of axial spondyloarthritis: a consensual approach by the ASAS/OMERACT MRI group. Ann Rheum Dis 2009; 68: 1520-7.
6. Sudoł-Szopińska I, Jurik AG, Eshed I, Lennart J, Grainger A, Østergaard M, et al. Recommendations of the ESSR arthritis subcommittee for the use of magnetic resonance imaging in musculoskeletal rheumatic diseases. Semin Musculoskelet Radiol 2015; 19: 396-411.
7. de Hooge M, van den Berg R, Navarro-Compán V, van Gaalen F, van der Heijde D, Huizinga T, et al. Magnetic resonance imaging of the sacroiliac joints in the early detection of spondyloarthritis: no added value of gadolinium compared with short tau inversion recovery sequence. Rheumatology 2013; 52: 1220-4.
8. Herregods N, Jaremko JL, Baraliakos X, Dehoorne J, Leus A, Verstraete K, et al. Limited role of gadolinium to detect active sacroiliitis on MRI in juvenile spondyloarthritis. Skeletal Radiol 2015; 44: 1637-46.
9. Gentili F, Cantarini L, Fabbroni M, Nigri A, Mazzei FG, Frediani B, et al. Magnetic resonance imaging of the sacroiliac joints in SpA: with or without intravenous contrast media? A preliminary report. Radiol Med 2019; 124: 1142-50.
10. Maksymowych WP, Lambert RG, Østergaard 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; 78: 1550-8.
11. Diekhoff T, Poddubnyy D, Proft F, Ziegeler K,

Deppe D, Niedermeier C, et al. New bone formation at the sacroiliac joint in axial spondyloarthritis: characterization of backfill in MRI and CT. Rheumatology 2023; 62: 3893-8.
12. Nygaard A, Jurik AG, Lund C, Schiøttz-Christensen B. The incidence of bone marrow oedema at the sacroiliac joints in a non-rheumatological population - a retrospective cohort study. BMC Musculoskelet Disord 2019; 20: 590.
13. Weber U, Jurik AG, Zejden A, Larsen E, Jørgensen SH, Rufibach K, et al. Frequency and anatomic distribution of magnetic resonance imaging features in the sacroiliac joints of young athletes: exploring "background noise" toward a data-driven definition of sacroiliitis in early spondyloarthritis. Arthritis Rheumatol 2018; 70: 736-45.
14. de Winter J, de Hooge M, van de Sande M, de Jong H, van Hoeven L, de Koning A, et al. Magnetic resonance imaging of the sacroiliac joints indicating sacroiliitis according to the Assessment of SpondyloArthritis International Society definition in healthy individuals, runners, and women with postpartum back pain. Arthritis Rheumatol 2018; 70: 1042-8.
15. Eshed I, Miloh-Raz H, Dulitzki M, Lidar Z, Aharoni D, Liberman B, et al. Peripartum changes of the sacroiliac joints on MRI: increasing mechanical load correlating with signs of edema and inflammation kindling spondyloarthropathy in the genetically prone. Clin Rheumatol 2015; 34: 1419-26.
16. Kiil RM, Weber U, Loft AG, Maimburg RD, Jurik AG. Evolution of magnetic resonance imaging lesions at the sacroiliac joints during and after pregnancy by serial magnetic resonance imaging from gestational week twenty to twelve months postpartum. Arthritis Rheumatol 2023; 75: 1166-75.
17. Renson T, Depicker A, De Craemer AS, Deroo L, Varkas G, de Hooge M, et al. High prevalence of spondyloarthritis-like MRI lesions in postpartum women: a prospective analysis in relation to maternal, child and birth characteristics. Ann Rheum Dis 2020; 79: 929-34.
18. Storey T, Borgia RE, Merritt P, Woolnough L. Normal magnetic resonance imaging appearance of marrow adjacent to the sacroiliac joints in children during development. J Comput Assist Tomogr 2022; 46: 91-6.
19. Borlandelli E, Ciaffi J, Festuccia G, Facchini G, Miceli M, Brusi V, et al. Osteitis condensans ilii: prevalence and characteristics of a neglected mimic of sacroiliitis. Clin Rheumatol 2022; 41: 483-90.
20. Mir R, Dragan AD, Mistry HB, Tsang YM, Padhani AR, Hoskin P. Sacral insufficiency fracture following pelvic radiotherapy in gynaecological malignancies: development of a predictive model. Clin Oncol (R Coll Radiol) 2021; 33: e101-9.
21. Wu YF, Lu K, Girgis C, Preda M, Preda V. Postpartum bilateral sacral stress fracture without osteoporosis-a case report and literature review. Osteoporos Int 2021; 32: 623-31.