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Latest Developments in Imaging for Axial Disease in Psoriatic Arthritis

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Introduction

Axial disease in psoriatic arthritis (axPsA), affecting the sacroiliac joints (SIJ) and spine, is recognized as one of the domains in the Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) treatment recommendations for psoriatic arthritis (PsA).[1] Accurate recognition of this manifestation is crucial for comprehensive management of this disease. It is defined according to both clinical and imaging features. Clinically, inflammatory back pain (IBP) is a key feature; however, findings from a recent Canadian inception cohort study—Screening for Axial Spondyloarthritis in Psoriasis, Iritis, or Colitis Cohorts 1 and 2 (SASPIC1 and 2)—which included patients with psoriasis and undiagnosed back pain, showed no differences in the frequency of IBP or non-steroidal anti-inflammatory drug (NSAID) responsiveness between those diagnosed with axPsA and individuals with other causes of chronic back pain.[2] Similarly, data from the global Axial Involvement in Psoriatic Arthritis (AXIS) cohort revealed only minor numerical differences in NSAID responsiveness or frequency of IBP, according to the ASAS criteria, between participants with and without axial involvement when evaluated by central reviewers.[3] Recent post-hoc studies of clinical trials in PsA have attempted to identify axPsA according to a Bath Ankylosing Spondylitis Disease Activity Index

(BASDAI) threshold of ≥4. However, MRI-based assessment of axPsA in a large European cohort of 581 PsA patients, recruited across 17 European registries within the EuroSpA network, indicated that a BASDAI ≥4 did not discriminate PsA patients with axial disease from those without.[4] Moreover, only 25–45% of patients with radiographic features of axPsA have been reported to have IBP, with some patients being clinically perceived as asymptomatic. Additionally, axSpA-based IBP criteria have demonstrated limited specificity for axPsA.[5,6] Studies using MRI have reported poor correlation between sacroiliitis on imaging and both the presence and type of back pain.[7,8]

Several radiographic features have been described that distinguish axPsA from axSpA based on cross-sectional studies that did not control for age, gender, or symptom duration, all of which may affect the radiographic appearance of the SIJ and spine. These features include less severe SIJ and spinal involvement compared to axSpA, reduced symmetry of sacroiliitis, asymmetry of spondylitis, and more frequent involvement of the cervical spine.[9] Data from the EuroSpA consortium indicated that radiographic sacroiliitis, as defined by the modified New York criteria (mNYc), was present in 29% of patients, which is comparable to the recent findings from the Canadian SASPIC cohorts.[2] Earlier studies had reported radiographic sacroiliitis per mNYc in 37% of Canadian patients with PsA,[10] 24% of British PsA patients,[11] and 29% of German PsA patients.[12] Additional reports included unilateral grade 2 sacroiliitis; using this lower threshold, a Canadian study reported axial involvement in 45% of PsA patients, while a German study reported a radiographic axPsA prevalence of 38%.[12,13] However, the SASPIC data did not demonstrate a significant difference in unilateral sacroiliitis between patients diagnosed with axPsA and those with PsA presenting with other causes of back pain. Moreover, the reliability of detecting low-grade radiographic sacroiliitis is poor, even among experienced musculoskeletal radiologists, making it a suboptimal criterion for defining axPsA.

Earlier studies have reported spondylitis in the absence of sacroiliitis in approximately 15% of cases. Bulky syndesmophytes, non-marginal syndesmophytes, and paravertebral bridging bone are often considered to be characteristic of axPsA compared to axSpA, although comparative data matched for age, gender, and symptom duration remain limited. Notably, the morphology of new bone formation in the spine has raised concerns that some cases designated as axPsA are in fact diffuse idiopathic skeletal hyperostosis (DISH). A Belgian study recently compared radiographic findings of the spine and SIJ in 525 patients (312 with PsA and 213 with SpA). Findings showed that patients with axSpA exhibited more severe spinal disease as indicated by higher modified Stoke Ankylosing Spondylitis (mSASSS) scores. In axPsA, syndesmophytes were more frequently observed in the cervical spine than in the lumbar segment.[14]

MRI is the cornerstone for diagnosis and disease classification in axial spondyloarthritis; however, few studies have systematically compared SIJ and spine findings between axSpA and PsA, especially in cohorts matched for symptom duration, age, and gender; factors which may influence MRI interpretation of the SIJ and spine. In a cross-sectional study of 125 cases from the Toronto cohort with IBP, only 44.6% demonstrated findings on MRI consistent with axSpA.[8] Another cross-sectional observational study from Brazil reported bone marrow edema (BME), enthesitis, erosions, and fat metaplasia on MRI in 37.8% of 45 cases diagnosed with PsA, most of whom were asymptomatic.[15] An Israeli cross-sectional study of 107 patients with PsA reported active sacroiliitis on MRI in 26%, with non-radiographic sacroiliitis evident in 11%.[16] In contrast, a retrospective Canadian cohort of 93 patients with PsA, 65 without axial symptoms and 28 with psoriasis with back pain, showed a lower prevalence of only 13%.[17] None of these studies reported detailed assessments of the type and distribution of MRI lesions.

The MAXIMISE study, a placebo-controlled trial of secukinumab in axPsA, published a secondary analysis in which the axial MRI scans were re-read to include inflammation of the posterior elements and degenerative changes, although no axSpA control group was included.[18] Patients were enrolled based on clinically diagnosed active axial disease (spinal pain ≥40/100 on the visual analogue scale and a BASDAI score ≥4/10). Approximately 60% of the patients had a Berlin BME score ≥1 for the spine and/or the SIJ, but it is unclear what proportion represented BME typical of axial inflammation as opposed to mechanical stress. This study reported inflammation of the spinous processes in 11.1% of axPsA cases (7.2% in the lumbar spine, 5.4% in the thoracic spine, and 2.1% in the cervical spine). In addition, imaging findings compatible with degenerative disease were observed in 64% of

patients, with 21.2% showing only degenerative findings on MRI. For structural lesions, assessment was limited to fat lesions in the spine.

A report from the EuroSpA consortium, which included 17 European registries and 581 patients with PsA, combined both radiographic and MRI evaluation of the SIJ in the routine evaluation of axPsA.[4] Among these, 208 cases (35.8%) had axSpA with psoriasis but without peripheral PsA. Experienced central readers judged the combined evaluation of pelvic radiographs and MRI as compatible with axPsA in 31%. This proportion was somewhat higher than the 23.2% imaging-positive rate for axPsA reported by central readers in the AXIS study[3] and the 17.6% observed in the SASPIC-2 Canadian cohort,[2] where all patients underwent MRI evaluation of the SIJ. These differences are likely due to the differences in study design: AXIS and SASPIC were inception cohorts, AXIS enrolled patients with PsA of <10 years duration and SASPIC included patients with psoriasis and chronic undiagnosed back pain, whereas the EuroSpA study was a convenience sample of PsA cases, nearly one third of whom had axSpA with psoriasis. The Berlin cohort, which had a similar study design as SASPIC-2, reported axPsA in 14% of patients. Among these, only eight had IBP, four showed radiographic sacroiliitis, and five had unilateral sacroiliitis grade ≥2. All cases demonstrated active inflammatory and/or structural (post)inflammatory changes in the SIJ and/or spine on MRI, and five only exhibited axial involvement of the spine.[12]

To date, only the EuroSpA consortium has reported a detailed assessment of the type and distribution of MRI lesions according to central reader evaluations using standardized definitions. Inflammatory lesions typical of axSpA were observed in 21% of patients, while BME overall was present in 44%, indicating that non-specific BME related to other causes, such as mechanical stress, was a common finding. Additional active lesions included inflammation within erosion cavities (8%), enthesitis (5.5%), capsulitis (4%), and joint space fluid (7%) in patients with axPsA. Structural SIJ MRI lesions indicative of SpA were observed in 28% of patients, with erosions (27%) and fat lesions (26%) being the most common. A notable observation that was also reported in the 2009 ASAS classification study of an inception cohort of cases with undiagnosed chronic back pain was the frequent co-occurrence of both inflammatory and structural lesions. Certain types of lesions, such as BME extending ≥1 cm from the subchondral bone, inflammation within an erosion cavity, capsulitis, fat metaplasia in an erosion cavity (backfill), and ankylosis were found almost exclusively in patients with axPsA. MRI findings indicative of SpA, including nearly all types of inflammatory and structural lesions except sclerosis, were more evident in males and HLA-B27 positive patients. Degenerative SIJ changes were observed in 16% of cases and represented the most common differential diagnosis, along with osteitis condensans ilii and mechanical stress-related BME. Multivariable analysis demonstrated that male gender, history of IBP, elevated CRP, and HLA-B27 positivity were independently associated with axPsA. Clinical and radiographic definitions of axial involvement in PsA overlapped only partially with MRI-based definitions, emphasizing the complementary role of clinical and imaging assessments.

Despite imaging data on axPsA remaining quite limited, several themes have emerged in recent years. First, clinical features alone, such as IBP, are not particularly helpful in identifying axial disease in patients with PsA, and only 30–40% of patients with axial disease are positive for HLA-B27. Second, radiography of the SIJ and spine is both insensitive and unreliable, with interpretation often confounded by age- and gender-associated changes, particularly given that axPsA develops later in life than axSpA. Third, MRI of the SIJ and spine is more sensitive than radiography, but interpretation may also be confounded by age, gender, and mechanical stress related to obesity. In particular, focal BME in the antero-inferior region of the SIJ is frequently observed in physically active and/or obese individuals, post-partum women within the first year after delivery, and in disorders such as DISH.

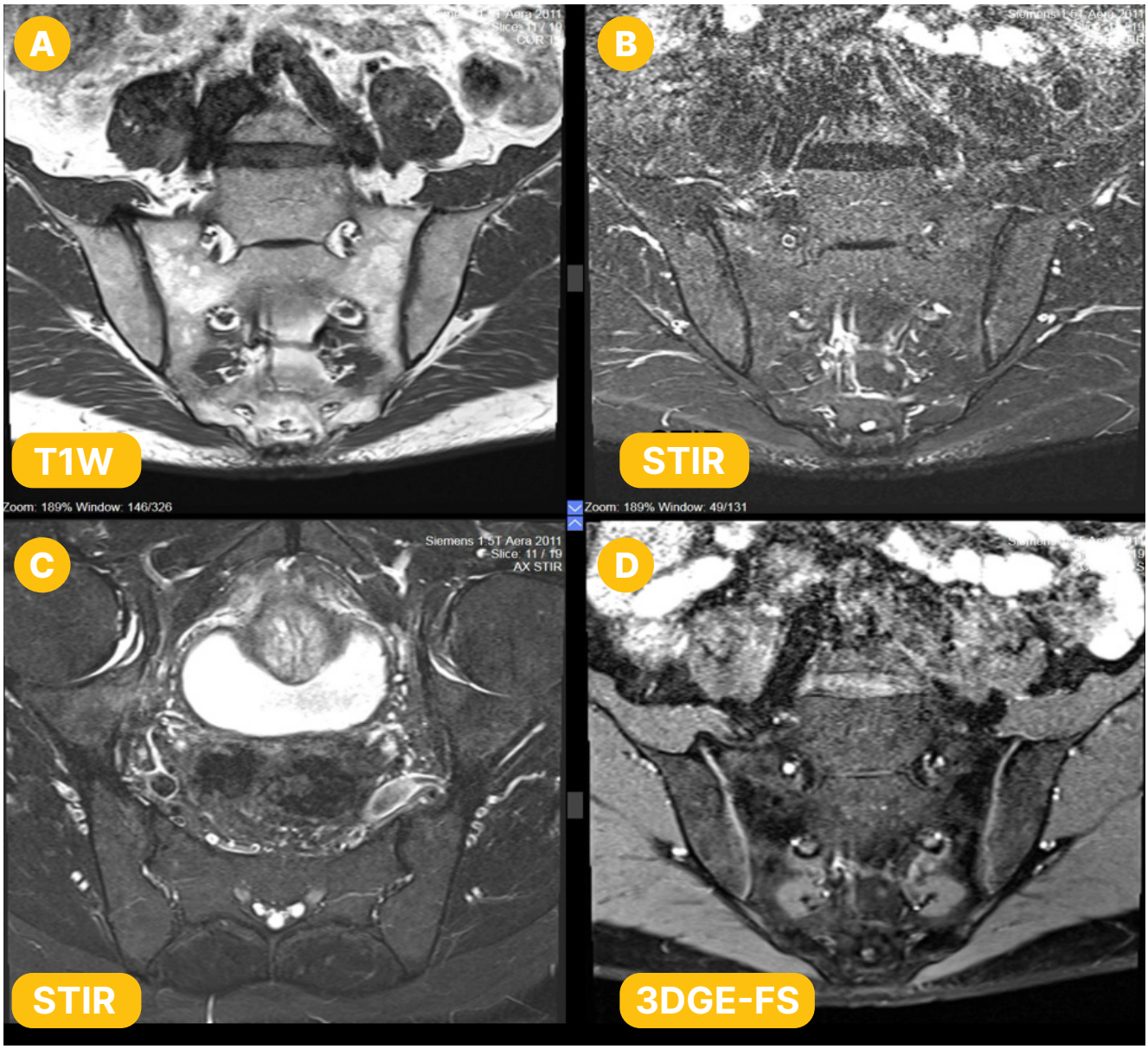

Figure 1. ASAS-SPARTAN standardised image acquisition protocol for diagnostic evaluation of the sacroiliac joints (SIJ).[19] **A)** Semicoronal T1-weighted fat-sensitive sequence. **B)** Short-tau Inversion Recovery (STIR) fluid-sensitive semicoronal sequence. **C)** STIR semiaxial sequence. **D)** Erosion sensitive thin slice sequence e.g. 3D-gradient echo; *courtesy of Walter P. Maksymowych, MB, ChB, MRCP (UK), FACP, FRCPC.*

Conclusion

Recent ASAS-SPARTAN recommendations call for the assessment of BME in both semicoronal and axial orientations using fluid-sensitive sequences that permit precise localization of the region with BME (**Figure 1**).[19] The presence of erosion or fat metaplasia enhances diagnostic specificity, and new MRI sequences are increasingly being implemented into routine evaluation of the SIJ. These thin slice, high-resolution sequences enhance the delineation of subchondral bone relative to the overlying cartilage or joint space, thereby offering superior performance compared to conventional T1-weighted sequences for detecting erosions[20] (**Figure 2**). Moreover, advanced sequences such as zero echo time (ZTE) and processing of data from 3D-gradient echo sequences can generate CT-like images, enhancing detection of both

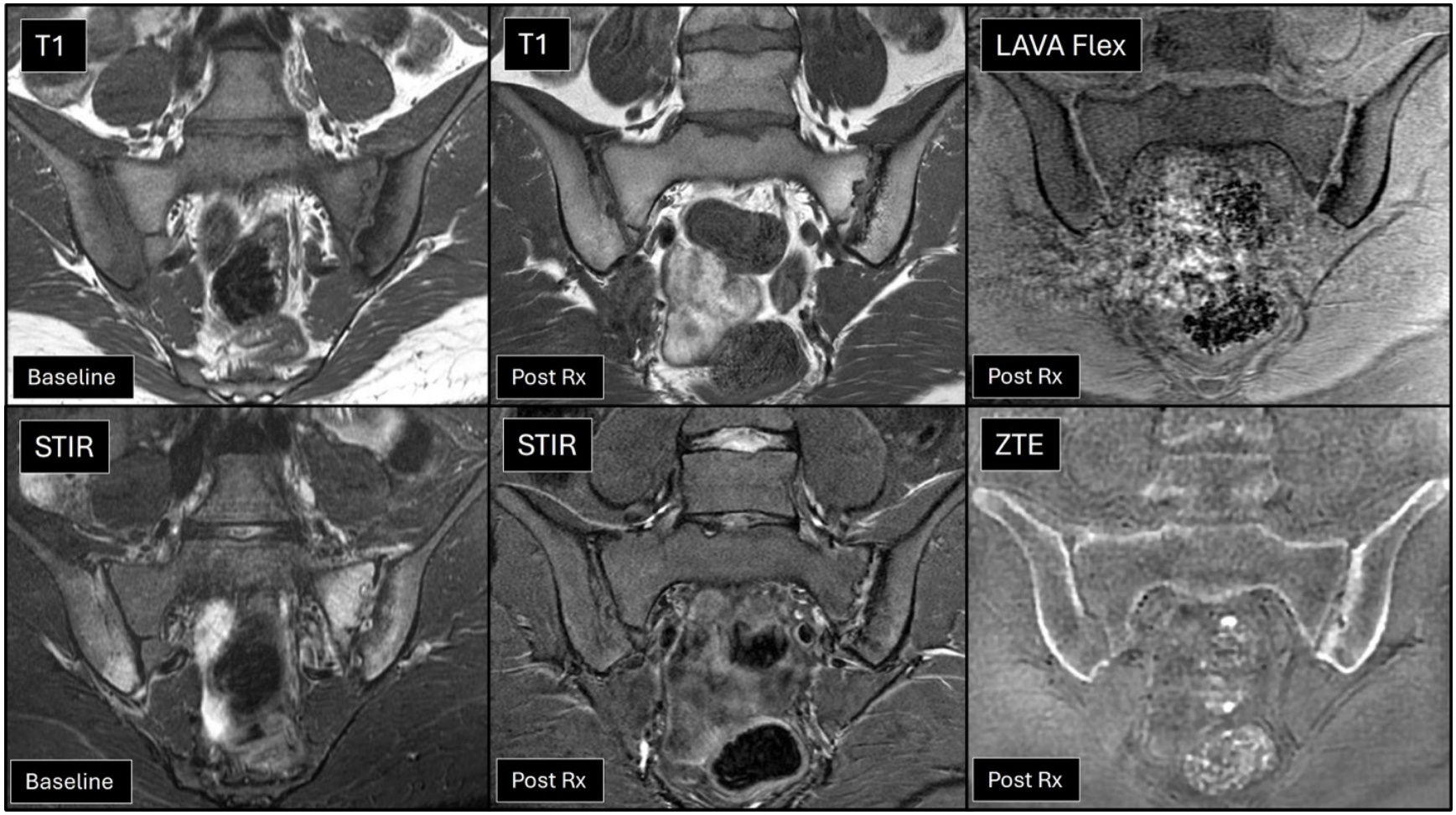

Figure 2. Sacroiliac joint (SIJ) MRI T1W, Short-tau Inversion Recovery (STIR) and 3D high-resolution scans.[20] STIR images confirm the presence of sacroiliitis with improvement in bone marrow edema after biologic therapy. At baseline, erosion is seen in the left iliac cortex that is less evident post-treatment on the T1W scan but more clearly evident on the high-resolution LAVA (liver acceleration volume acquisition) Flex and zero echo time (ZTE) sequences. (Rx: therapy); *courtesy of Walter P. Maksymowych, MB, ChB, MRCP (UK), FACP, FRCPC*.

erosions and new bone formation in the SIJ and spine (**Figure 2**). Increasingly, MRI assessment of the SIJ and spine for both inflammatory and structural lesions should be considered the standard of care in PsA patients with chronic undiagnosed back pain, particularly if the patient is sufficiently symptomatic to warrant consideration of disease-modifying antirheumatic drugs effective for axial disease.

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