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SPONDYLOARTHRITIS (M KHAN AND N AKKOC, SECTION EDITORS)

Imaging in Axial Spondyloarthritis: What is Relevant for Diagnosis in Daily Practice?

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Abstract

Purpose of Review To explore how imaging may assist diagnosing axial spondyloarthritis in rheumatology practice.

Recent Findings A diagnosis of axial spondyloarthritis is based on pattern recognition by synthesizing clinical, laboratory, and imaging findings. In health care settings providing low threshold access to advanced imaging, sacroiliac joint MRI is the preferred imaging modality in clinically suspected axial spondyloarthritis. In daily routine, the optimum protocol to assess suspected inflammatory back pain combines sacroiliac joint and spine MRI fitting a 30-min slot. Contextual assessment of concomitant structural and active MRI lesions is key to enhance diagnostic utility. In women with postpartum back pain suggestive of axial spondyloarthritis, recent reports advocate waiting 6–12 months after delivery before acquiring sacroiliac joint MRI. Major unmet needs are consistent MRI protocols, standardized training modules on how to evaluate axial MRI, and timely dissemination of imaging advances into mainstream practice both in rheumatology and in radiology.

Summary In rheumatology practice, MRI has become indispensable to help diagnose early axial spondyloarthritis. However, major gaps in training and knowledge transfer to daily care need to be closed.

Keywords Spondyloarthritis · Ankylosing spondylitis · Imaging · Magnetic resonance imaging · Diagnosis · Rheumatology practice

Introduction

In routine care, making a diagnosis of early axial spondyloarthritis (SpA) among the common disorders of mechanical back pain remains challenging [1, 2]. The diagnostic approach in this systemic inflammatory condition known for its protean manifestations relies on complex pattern recognition by integrating clinical, laboratory, and imaging findings. This multidimensional process often results in varying levels of confidence with a diagnosis of axial SpA, which requires re-appraisal according to disease evolution upon follow-up.

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The use of the Assessment of SpondyloArthritis international Society (ASAS) classification criteria [3] to diagnose axial SpA in daily practice is strongly discouraged due to the inherent risk of overdiagnosis and potentially harmful overtreatment when applied to unselected and not yet diagnosed individuals with persistent back pain [4]. The pre-test probability of classification criteria developed in tertiary care aiming at high specificity to recruit a homogenous study sample for research purposes is discrepant from routine care settings. An overcall bias by using classification criteria for diagnostic purposes in the primary care setting is exemplified by an observational cohort of 364 patients with chronic back pain recruited from primary care, where every fourth subject met the entry criterion of the ASAS classification criteria for axial SpA [5]. Two-thirds of these individuals also fulfilled the ASAS MRI definition of sacroiliitis, but only 20% were positive for HLA-B27, indicating the presence of nonspecific sacroiliac joint (SIJ) bone marrow edema (BME) in most subjects.

A major task in routine clinics is an evaluation towards potential differential diagnostic conditions, which does not apply to classification criteria to be used in individuals already diagnosed with a given disorder. As in many systemic diseases in rheumatology, we lack diagnostic criteria for axial SpA. Professional societies such as the American College of Rheumatology do not endorse diagnostic criteria in conditions of unknown causation since no gold standard is available to validate candidate criteria [6]. This leaves the clinician in a dilemma in conditions of diverse "gestalt" such as axial SpA.

In recent years, advanced imaging has emerged as a promising tool to assist clinicians in diagnosing axial SpA in daily routine. However, most publications about imaging in axial SpA were designed for research or classification purposes. Translating these research findings into daily practice means navigating through largely uncharted terrain because of limited evidence and discrepant settings in research and daily routine. This article highlights recent progress about how to use imaging in axial SpA in daily practice and addresses key issues to advance the field. The article does not discuss scintigraphy, which is little used in general rheumatology practice, and very little published data is currently available regarding use of low-dose CT for axial SpA.

Why Has Imaging Become That Prominent in Early Diagnosis of Axial Spa?

Clinical and laboratory evaluation have limited utility in early recognition of axial SpA. The discriminative capacity of inflammatory versus mechanical back pain features from patient history is virtually exhausted by their use as referral criteria from primary care to rheumatologists [7, 8]. Moreover, fewer than one-third of patients with new-onset inflammatory back pain progressed to spondyloarthritis during a follow-up of >13 years in a population-based study, while symptoms resolved in almost one-half of the patients [9•]. In rheumatology practice, inflammatory back pain criteria [10] and clinical examination have marginal diagnostic value. The SIJs are barely accessible to physical examination, and none of a plethora of SIJ pain provocation tests proposed to recognize sacroiliitis has proven clinically meaningful specificity or inter-rater reliability [11, 12]. Spinal mobility measures in patients with recent-onset back pain could not discriminate between inflammatory and non-inflammatory back pain [13]. Likewise, laboratory examination and pelvic radiography contribute little to early recognition of axial SpA, mainly due to their limited sensitivity in early disease. In daily routine, HLA-B27 has limited diagnostic value as well given its background prevalence of about 6–10% in Europe [14, 15]. Obesity, a common condition in rheumatology care, is associated with increased C-reactive protein levels, particularly in women [16, 17]. Repeated measurements of C-reactive protein should be considered in case of an initially normal value in early axial SpA [18]. Limitations affecting all domains of routine clinical examination raised expectations whether imaging may enhance diagnostic confidence in clinically suspected early SpA in daily care [19, 20].

What Constitutes a Diagnostic SIJ MRI if Axial SpA Is Clinically Suspected?

Contextual Assessment of Concomitant Structural and Active MRI Lesions Is Key to Enhance Diagnostic Utility in Daily Practice

A generic requirement to assess imaging in SpA in daily routine is familiarity with the MRI lesion spectrum observed in the axial skeleton in patients with SpA. ASAS has recently published consensual SIJ lesion definitions illustrated by reference images for each lesion type [21••]. Spine MRI lesion definitions accompanied by an atlas of reference images have been updated as well by the Canada-Denmark MRI in SpA working group [22••]. The MRI lesion signature spanning from early bone marrow edema to structural changes such as fat metaplasia or erosion, transitioning to ankylosis in some patients, reflects the complex bone remodeling cascade featuring inflammation, bone resorption, and osteoproliferation in axial SpA. Erosion as a highly specific lesion type can reliably be detected in 60–90% of patients with incipient axial SpA as short as 2 years after symptom onset [23–25].

An updated ASAS consensus designed for research purposes defined SIJ BME "highly suggestive" of SpA as the cardinal MRI feature to classify active sacroiliitis [26]. In case of suspected early axial SpA in daily practice, focusing on solitary MRI features such as BME alone rather than on the

entire inflammatory lesion trajectory is often misleading. In many controlled studies, the presence of SIJ BME has consistently been reported in 20–30% of healthy individuals and of patients with mechanical back pain [23, 27–37], and in up to 41% of athletes, where the ASAS criterion of a positive SIJ MRI was met according to the assessment by majority of experienced readers [38]. Lumbosacral transitional anomalies simulating sacroiliitis represent another confounder relevant to daily practice [39]. This aggregate evidence substantiates the limited specificity of SIJ BME alone to discriminate SpA from non-SpA back pain patients in daily care, unless the BME is fairly extensive.

Anatomical location and size often matter regarding specificity of BME lesions. BME in the posterior lower ilium or in the upper anterior sacrum is of particular concern in daily practice, since it is frequently observed in athletes and healthy individuals [34, 38]. Potential explanations are anatomical SIJ variants, repetitive axial strain injury, incipient osteoarthritis, or partial volume averaging from vascular signals simulating BME. Clustered small BME lesions in the SIJ proved to be a common finding in patients with mechanical back pain [31]. By contrast, extended ("deep") SIJ BME changes taking at least one-third of the volume of a SIJ quadrant were found to be better predictive of the evolution of axial SpA upon follow-up over 4–8 years, respectively [40–42].

However, also small BME lesions not dissimilar to changes seen in mechanical back pain patients or healthy individuals can be indicative of active sacroiliitis, if located around an unequivocal SIJ erosion [43]. By contrast, even extended SIJ BME lesions in a clinical setting suggestive of early axial SpA can be misleading without taking into account the differential diagnostic clinical context, in particular in the absence of structural SIJ lesions. This pitfall in daily routine is illustrated by a growing number of case reports about mimickers of SpA-related extensive SIJ BME ranging from crystal arthropathies inclusive of tophaceous gout and calcium pyrophosphate deposition disease to reactive arthritis, insufficiency fractures, septic arthritis, IgG4-related disease, sarcoidosis, hematologic conditions, and neoplastic disorders such as osteoblastoma or lymphoma [44–52].

In daily routine, single-lesion assessment of SIJ MRI restricted to BME is conflicting. The intersection between disease-specific BME and background signal variation observed in healthy individuals or patients with mechanical back pain has not been determined. Moreover, such an approach neglects the more specific incremental information derived from the early appearance of structural lesions. These biases can be overcome by contextual assessment of SIJ MRI [30, 35, 36, 53–55]. This approach aims to extract the contextual information provided by concomitant structural and BME lesions by scrolling simultaneously across complementary T1 spin echo (T1SE) and short tau inversion recovery (STIR) sequences of SIJ MRI. The significance of any changes on one sequence is often modified by the presence or absence of other lesion types on a complementary sequence, which minimizes the risk of biased assignments based on isolated or subtle lesions observed on just one sequence.

Should Classification Thresholds of MRI Lesions Be Applied in Daily Routine?

Various MRI thresholds defining a minimum number of active and/or structural SIJ lesions needed to discriminate early axial SpA from mechanical back pain have been proposed [30, 56]. ASAS recently reported SIJ lesion cutoffs for application in disease classification meeting a specificity of ≥0.95, which were validated for positive predictive validity ≥95% for rheumatologist diagnosis in a subsample by clinical and MRI follow-up over median 4.4 years [57••]. All cutoffs were derived from cohorts referred to specialized tertiary care clinics.

The use of lesion thresholds for diagnosis in daily routine may not be appropriate since many determinants to develop cutoffs for classification are divergent from routine care mainly because of discrepant pre-test probability between the settings of specialized tertiary care and daily routine. However, the recently reported ASAS SIJ lesion cutoffs were derived from an analysis which used majority central reader decision that an MRI scan had BME considered highly suggestive of axial SpA as the gold standard. BME in ≥3 consecutive slices or in ≥4 SIJ quadrants had ≥95% specificity for BME considered highly suggestive of axial SpA. It is to be expected that this would be the same irrespective of whether the scan is derived from a patient in a community-based setting or attending a tertiary care facility. The positive predictive value of such cutoffs for a diagnosis of axial SpA will depend on the pre-test probability of axial SpA in the study population but this approach to deriving meaningful cutoffs may be one solution to the challenges posed by ascertaining a final diagnosis and the selection of appropriate controls. Finally, these recent data-driven lesion cutoffs on SIJ MRI are a call to abandon the widespread misuse of the quantitative component of the ASAS definition of a positive SIJ MRI, comprising BME in ≥2 locations on one slice or in one location on ≥2 consecutive slices, as a diagnostic criterion for axial SpA [57, 58].

Evidence-Based Recommendations on the Use of MRI for Diagnosing Axial SpA in Routine Rheumatology Care

Interpretation of imaging or laboratory biomarkers depends on the pre-test probability of the suspected condition determined by clinical assessment. In daily practice, evaluation of SIJ MRI detached from the clinical context carries a high risk of bias. SIJ MRI may have substantial diagnostic utility in axial SpA by assisting clinical judgment in routine practice, but

MRI findings in isolation cannot supplant clinical reasoning. Another confounder is the undetermined intersection between physiological background noise and disease regarding lesions such as BME or fat metaplasia.

The British Society for Spondyloarthritis developed evidence-based recommendations on the use of MRI in the diagnosis of axial SpA by a systematic literature review followed by an anonymized Delphi process [59, 60]. This consensual approach jointly by rheumatologists and radiologists aimed at standardizing daily practice and reducing heterogeneity around the use of MRI in suspected axial SpA. The authors agreed on an overarching principle that the diagnosis of axial SpA is based on clinical, laboratory, and imaging features. Two key recommendations reaching high agreement were "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" and "In the SIJs, the presence of bone marrow edema, 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." These statements emphasize the quintessential role of contextual assessment of concomitant structural and active MRI lesions to further the diagnostic process of axial SpA in daily practice. Essential unmet needs identified by the British working group were standardized MRI acquisition protocols for clinically suspected axial SpA and standards for reporting MRI features to facilitate information transfer among radiologists and rheumatologists.

Clinically Suspected Axial SpA, but Negative SIJ MRI — How to Proceed?

Normal or inconclusive findings on SIJ MRI do not rule out clinically suspected axial SpA. Subjects with indeterminate SIJ MRI despite clinically suspected axial SpA need follow-up visits in rheumatology practice. However, evidence is limited whether and when to repeat SIJ MRI. Spontaneous fluctuation in SIJ BME with new-onset BME in 15% and resolution of initial BME in 30% was observed in 68 patients suspected to have axial SpA, who were monitored by annual SIJ MRI over 2 years [61]. In 2 prospective studies over 12 weeks, new-onset sacroiliitis was reported in 9.3% and 5.3% of patients with suspected early axial SpA, respectively [62, 63]. In a cohort of patients with chronic back pain where BME alone served as outcome parameter, 16.5% showed ASAS-positive SIJ MRI at baseline, while 7.2% switched from negative to positive upon the 12-month follow-up [64]. Transferring these findings into clinical practice is restrained by numerous study limitations such as small sample size, short observation period, post hoc analysis, lack of controls, or selecting BME alone as endpoint. An approach derived from clinical experience may be to repeat SIJ scans either upon a subsequent flare of back pain or after an interval of 6–12 months, dependent on the degree of patient symptoms and whether a change in management is contemplated.

Prime Time to Substitute Pelvic Radiography by SIJ MRI

In daily routine, pelvic radiography is the traditional imaging modality in axial SpA despite limited evidence whether radiography may enhance diagnostic confidence in early disease. Radiographic SIJ evaluation according to the modified New York criteria was derived from patients with advanced SIJ damage [65, 66]. Substantial limitations such as low sensitivity in early disease, radiation exposure in early adulthood, or notoriously poor reliability [67, 68] even resulting in opposite sensitivity to change [69, 70] culminated in the claim to abandon pelvic radiographs in the assessment of back pain patients with clinically suspected early axial SpA [53] (Fig. 1).

Head-to-head comparisons of pelvic radiographs and SIJ MRI and of both imaging modalities and low-dose CT as reference standard consistently favored SIJ MRI by its superior sensitivity and reliability, on top of depicting both active and structural SIJ lesions by the cross-sectional imaging technique. Assessment of SIJ MRI according to the ASAS definition in back pain patients clinically suspected to have axial SpA showed superior kappa agreement of 0.73 [71] compared to only 0.54 by radiographic SIJ evaluation [67]. A systematic comparison of both imaging techniques against low-dose CT of the SIJ as gold standard demonstrated higher sensitivity for structural SIJ lesions and superior inter-reader reliability favoring SIJ MRI [72]. Low-dose CT may be a second-line imaging option in daily routine in settings such as difficult-to-assess pelvic radiographs, radiographic suspicion of erosions in conjunction with osteitis condensans ilii, in case of suspected anatomic SIJ variation or equivocal lesions on T1SE SIJ MRI [73].

Pelvic radiography is recommended as the primary imaging modality by the European League Against Rheumatism (EULAR) and the European Society of Musculoskeletal Radiology for diagnosis and management of axial SpA in rheumatology practice [74, 75]. Accumulating evidence calls for a critical re-appraisal of using pelvic radiographs as the first imaging choice for clinically suspected early SpA. In health care systems providing low threshold access to advanced imaging, SIJ MRI should be the preferred imaging modality in early axial SpA, especially in women of childbearing age or if a major treatment decision is contemplated. Such a paradigm shift requires training and competence in interpretation of SIJ MRI.

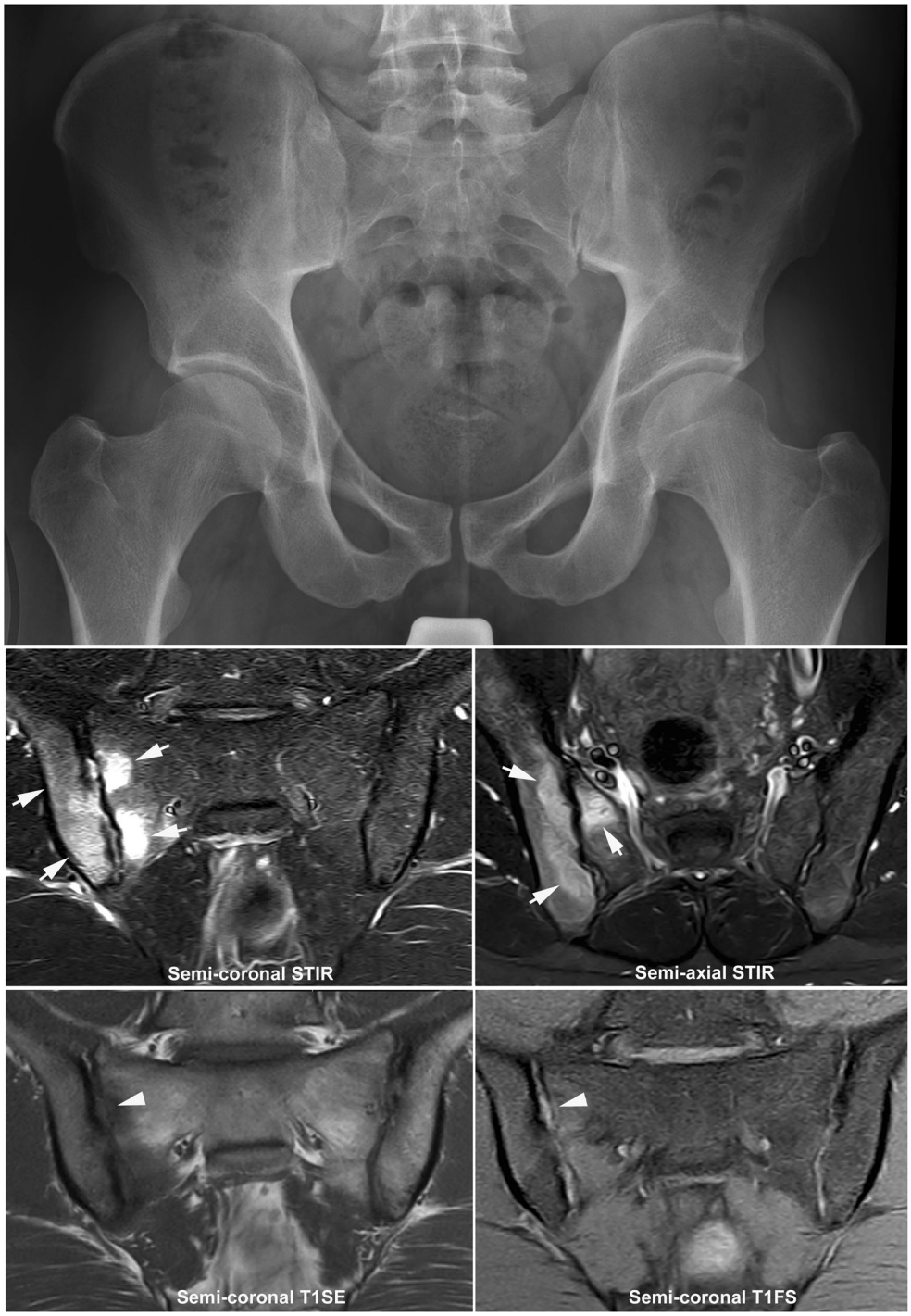

Fig. 1 Superior diagnostic utility of SIJ MRI versus pelvic radiography in early axial spondyloarthritis. A thirty-one-year-old HLA-B27-positive man referred for right-sided low back, hip, and buttock pain for 7 months, normal CRP. A pelvic radiograph ordered for initially suspected hip dysplasia shows no relevant changes of the hips or SIJs. SIJ MRI 4 weeks later with semi-coronal STIR/T1SE/T1FS and semi-axial STIR sequences reveal florid right-sided sacroiliitis (arrows) with concomitant large erosion (arrowhead) in the right sacrum only a couple of months after symptom onset. This figure illustrates the diagnostic superiority of SIJ MRI in early disease compared to traditional assessment by pelvic radiography

Hot Topics in Imaging Research in SpA Which Impact Clinical Decision-making

Emerging Evidence on Pregnancy-Related Signal Alterations on SIJ MRI

In recent years, data deficiency about peripartum and postpartum lesions on SIJ MRI emerged as a major challenge in rheumatology practice. In a cross-sectional study, 41% of women with postpartum buttock pain persisting for 4–16 months after delivery still met the ASAS definition of sacroiliitis [76]. The prototypic clinical vignette is a woman presenting with persisting back pain indicative of inflammatory origin for several months postpartum (Figs. 2). Is this a consequence of peripartum and postpartum mechanical strain, or could mechanical triggers during pregnancy unmask axial SpA in genetically prone individuals? Is back pain linked to SIJ MRI changes or are postpartum SIJ lesions common and

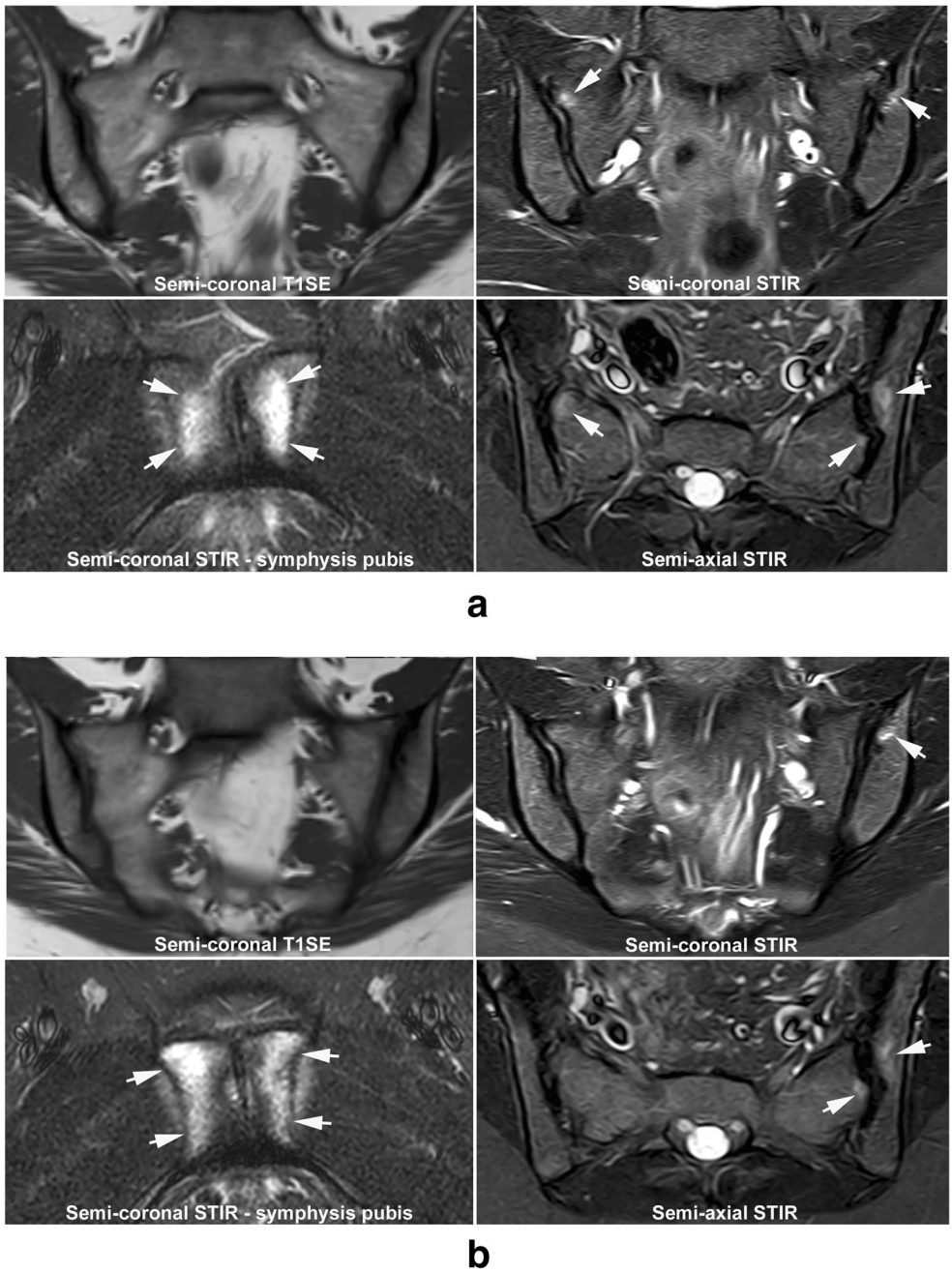

Fig. 2 Evolution of postpartum changes on SIJ MRI. A thirty-one-year-old woman with persisting low back and hip pain after her first pregnancy, worse with physical activity, neither pain at night nor morning stiffness; CRP normal, HLA-B27-negative. **a** Three months after childbirth, SIJ MRI with semi-coronal T1SE/STIR, and semi-axial STIR sequences, plus semi-coronal STIR scans of the pubic symphysis show subchondral edema at the upper part of both SIJs and pronounced bone marrow edema in the symphysis (arrows) in the absence of structural lesions. **b** Twelve months after delivery, subchondral edema in the SIJ has regressed to a residual lesion in the upper left SIJ (arrows), while symphyseal edema is virtually unchanged (arrows)

mostly asymptomatic findings, possibly associated with anatomical SIJ variants? Is there a difference in back pain or MRI lesions after a first delivery or multiple pregnancies? Are imaging features dependent on the mode of delivery? MRI lesions in the SIJ for a couple of weeks after delivery are widely regarded as transient consequence of mechanical strain during pregnancy. However, an unresolved issue in rheumatology practice is for how long postpartum an assessment towards potential axial SpA is justified, provided there are persistent features indicative of inflammatory back pain and/or BME-like MRI signals around the SIJ. This common clinical dilemma collides with data deficiency about the evolution of peripartum and postpartum lesion signature on SIJ MRI over 1 or 2 years after delivery.

Two recent reports applying different methodology provided preliminary insights into this controversy. A Belgian prospective study investigating the evolution of postpartum SIJ MRI lesions obtained serial SIJ MRI ≤10 days after delivery, at 6 months and only for women having an ASAS-positive MRI also at 12 months [77••]. The sample size was relatively small with 35 women who had a mean age of 29.7 years. For the 3 timepoints, the ASAS definition for active sacroiliitis was met by 60%, 15%, and 12% of women, respectively. Over 12 months of follow-up, virtually no structural MRI

lesions evolved; BME converted into fat metaplasia in only 9% of study subjects. A cross-sectional study from France used a different study design [78•]. Pelvic MRI of 423 women referred to imaging for gynecologic conditions, not for musculoskeletal disorders, were assessed and stratified into 3 groups: early (≤12 months) and late (≥24 months) postpartum versus nulliparous women. ASAS-positive sacroiliitis was reported in 25%, 17%, and 10% of women, respectively. Consistent with the Belgian study, erosion was uncommon, observed in 7%, 6%, and 5% of cases, respectively.

These aggregate findings suggest a declining gradient of SIJ BME over 6–12 months postpartum indicating a wait period of 6–12 months before acquiring SIJ MRI in women with postpartum back pain suggestive of axial SpA. However, there is no data about how long usually transient postpartum BME may persist in a minority of women potentially confounding SIJ MRI lesion signature also over longer periods than just 12 months. Moreover, appropriate re-testing by MRI should not be deferred by 6–12 months in highly symptomatic women, where interpretation of MRI scans is preferentially focused on emerging structural lesions.

A second clinically relevant feature shared by both reports is the striking paucity of erosion observed despite the high frequency of ASAS-positive sacroiliitis in postpartum women, highlighting the high specificity and thus key relevance of structural lesions on SIJ MRI towards recognition of early axial SpA.

Osteitis Condensans Ilii: Easy to Identify or Overlooked Complexity?

Interest in this common feature on pelvic radiographs has recently raised as to whether adjacent BME or erosion on SIJ MRI occurs in conjunction with osteitis condensans ilii (OCI) or may reflect co-occurrence of recent-onset axial SpA [79, 80]. Another matter of debate is whether incident OCI could be associated with anatomical SIJ variants which may generate BME.

A retrospective matched case-control study compared the prevalence of SIJ MRI lesions in 27 subjects with OCI and chronic back pain versus 27 patients with definite axial SpA [81]. There was no difference in the prevalence of SIJ BME in the OCI and axial SpA groups (93% versus 85%, respectively), but erosion was much less common in OCI (7% versus 67%). Virtually all lesions in OCI were observed in the anterior SIJ as opposed to axial SpA where lesions were predominantly located in the center of the articular surface.

In daily routine, BME on SIJ MRI associated with OCI remains a differential diagnostic dilemma. Discrimination from incident axial SpA mainly relies on the clinical context, on concomitant structural MRI lesions specific for axial SpA and in selected cases on serial MRI examinations or additional low-radiation CT (Fig. 3).

Is Spine MRI Part of a Routine Clinical Evaluation of Suspected Axial SpA?

In back pain patients clinically suspected to have axial SpA, but with inconclusive SIJ MRI, an increase in sensitivity by additional spine MRI to SIJ MRI was offset by a loss in specificity of similar magnitude resulting in no incremental diagnostic utility over SIJ MRI alone [82]. In 2 cohorts of patients with persistent back pain, spinal inflammation without evidence of sacroiliitis was observed in only 1–2% of patients, a minimal extra yield for classification according to the ASAS criteria [83]. Several proposals to define lesion thresholds on spine MRI aiming at a specificity of ≥0.90 for axial SpA showed a considerable spread of suggested cutoffs [56, 84–87] depending on various factors such as selection of controls, the gold standard used for classification, the characteristics of study subjects such as age group and symptom duration, or the high background frequency of vertebral corner lesions in the general population possibly associated with age and axial strain [88] or in patients with mechanical back pain [30, 35]. Another confounding factor is the common presence of degenerative spinal MRI lesions in up to 90% of young subjects both with and without axial SpA [89, 90].

Which lessons relevant to daily practice can be derived from this data about spinal MRI changes? Investigating persisting low back pain in young adults by spine MRI only under the assumption of a degenerative disorder has a high risk of overcalling axial SpA, mainly due to the background noise of frequent nonspecific vertebral corner lesions in the general population. In this diagnostic scenario, an additional SIJ MRI is recommended due to superior specificity of the SIJ lesion signature. An additional spine MRI in case of equivocal SIJ MRI in subjects clinically suspected to have axial SpA generally has little incremental utility towards a diagnosis of axial inflammation. A supplementary spine MRI may be ordered if symptoms are present in locations beyond the buttocks such as low back or interscapular pain or in patients with suspected or evident psoriatic arthritis. However, an extra spine MRI has most value in the differential diagnosis of alternate non-inflammatory back pain by re-directing the clinical assessment towards degenerative conditions of the spine, lumbosacral transitional anomalies mimicking inflammatory back pain, or metastatic or septic disorders of the axial skeleton simulating a flare of axial SpA. Reviewing these deliberations, the British Society of Spondyloarthritis recommended to routinely acquire combined SIJ and spine MRI [59••]. The software of modern MRI devices operates to scan SIJ and spine together fitting a standard slot of 30 min. This approach saves the extra time and administrative costs of a subsequent separate referral to spine MRI after scanning the SIJ alone.

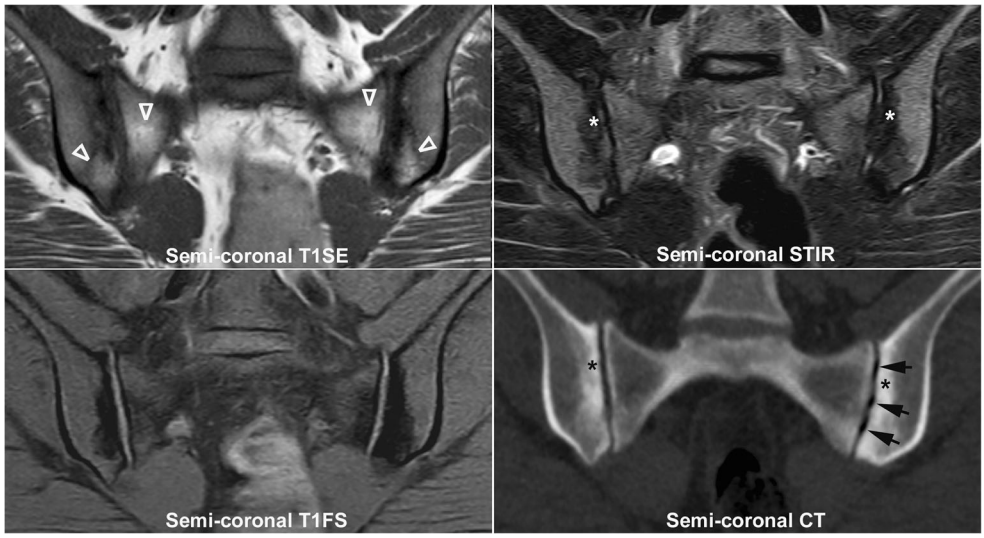

Fig. 3 Nonspecific MRI lesions in conjunction with osteitis condensans ilii. A twenty-six-year-old woman with low back pain for 2–3 years irradiating to the right buttock and leg. The pain had both inflammatory and non-inflammatory characteristics being worst at night and improving by exercise. The pain aggravated after her first childbirth 18 months previously. She was suffering from morbid obesity with a BMI of 41 kg/m^2, which may be a confounder for the interpretation of elevated CRP levels [16]. CRP 18 mg/l (reference <8.0 mg/l), HLA-B27 negative. SIJ MRI with semi-coronal T1SE, STIR, and T1FS images and a semi-coronal CT reconstruction show subchondral sclerosis (asterisk) and fat metaplasia (arrowheads) in both iliac bones and to a lesser extent in the sacrum, but no erosions. The appearances of the fatty lesions on T1SE MRI are not characteristic of post-inflammatory fat metaplasia compatible with the ASAS consensual definition [21••]. The CT reveals subchondral sclerosis (asterisk) and vacuum phenomena in the joint cavities (black arrows) reflecting degenerative changes

A Roadmap to Advance MRI in Axial SpA in Daily Routine

MRI is a powerful tool to assist evaluation of patients with clinically suspected axial SpA. However, a number of critical issues such as consistent MRI protocols, training how to evaluate axial MRI and disseminating advances to daily practice of rheumatologists and radiologists, institutionalized collaboration between the 2 specialties, and reporting of MRI findings using a shared standardized terminology ought to be addressed to enhance the use of axial MRI in daily routine.

Surveys Exploring Radiology and Rheumatology Practice

In an online survey among consultant radiologists in the UK [91], most SpA MRI protocols were not consistent with a consensus statement by the European Society of Skeletal Radiology [92]. Ninety-six percent of radiologists had implemented contextual assessment of axial MRI to assist making a diagnosis of axial SpA, highlighting the relevance of combined structural and active lesions in daily radiology practice.

Sacroiliitis and degenerative spine disease were the most common indications to request axial MRI according to an online survey among practicing rheumatologists in member countries of the EULAR [93•], but only 13% of rheumatologists reported reading MRI themselves.

MRI Protocols

MRI in patients with suspected axial SpA should comprise MRI of the SIJ and in most instances also of the spine. There is no standard acquisition protocol. SIJ MRI should be performed with T1-weighted and highly fluid-sensitive sequences (usually STIR sequence) in semi-coronal plane tilted parallel to the long axis of the sacrum. A standardized SIJ protocol is applied in a global initiative to evaluate classification criteria for axial SpA under the auspices of ASAS and Spondyloarthritis Research and Treatment Network, which can be downloaded at www.carearthritis.com/service/mri-spa-imaging-acquisition-protocols/.

Amending semi-axial STIR sequences taking about 4 extra minutes substantially reduced false-positive assignments of ASAS-positive sacroiliitis based on BME on semi-coronal plane alone by unmasking features such as partial volume averaging by vessel signals mimicking BME [94]. Moreover, additional semi-axial scans are instrumental to detect anatomical SIJ variants triggering nonspecific BME, 2 common variants being accessory joints in the posterior compartment [95–98] and the iliosacral complex [99] (Figs. 4). Anatomical SIJ variants simulating disease uncovered by perpendicular MRI slice orientation were confirmed by histology specimens [100]. Expensive gadolinium-enhanced SIJ scans provided no incremental diagnostic utility over STIR sequences alone and are generally not recommended in daily practice [101–103]. Scanning the cartilaginous joint compartment is adequate; incorporation of the ligamentous

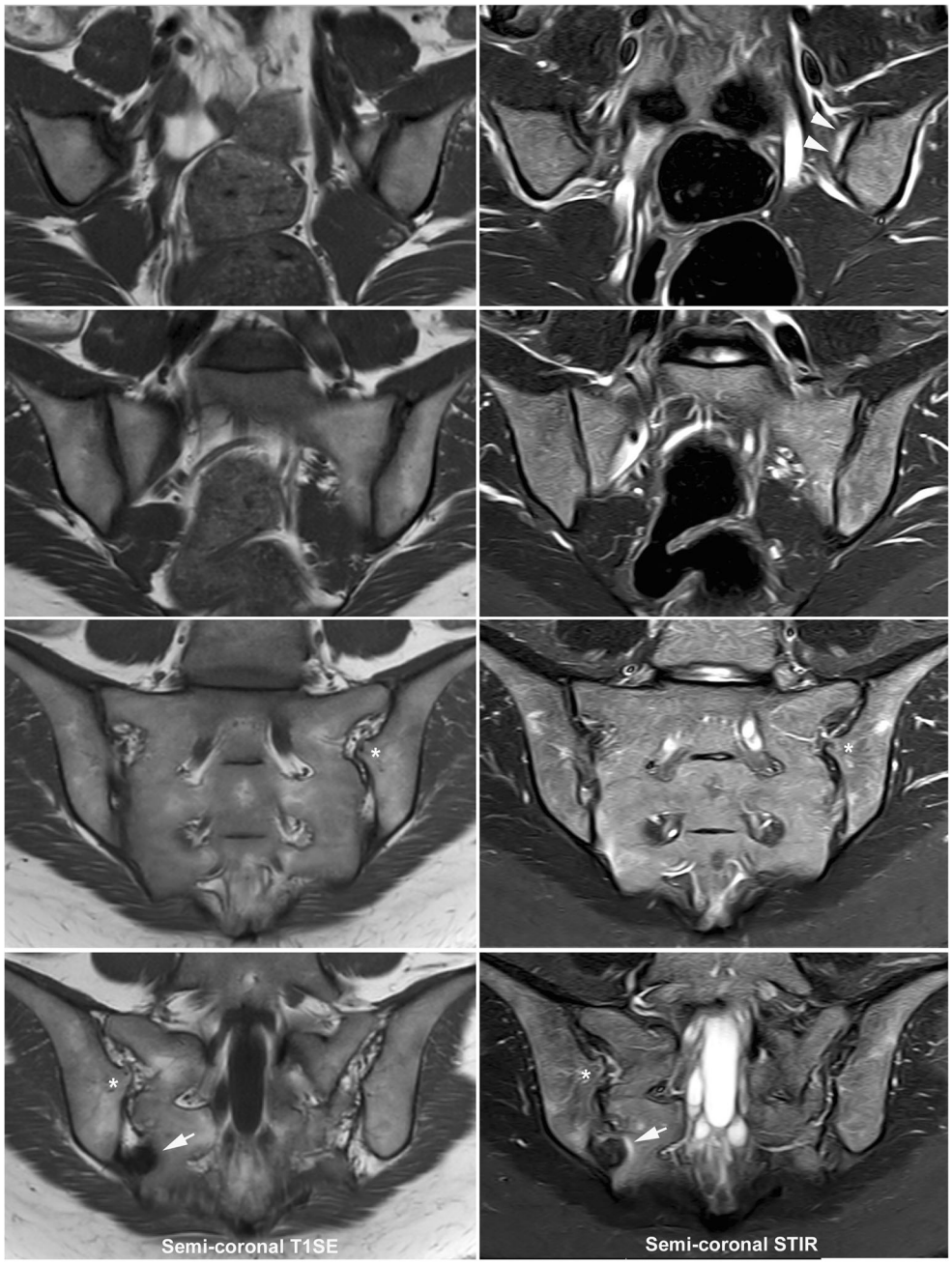

Fig. 4 Anatomical SIJ variants simulating BME on MRI: accessory joint and iliosacral complex. A 25-year-old woman with low back and buttock pain for 6 months. CRP normal. HLA-B27 not determined. **a** SIJ MRI with semi-coronal T1SE and STIR images shows a right-sided accessory joint located in the posterior inferior SIJ with surrounding bone marrow edema (arrows) and symmetrically an iliosacral complex (asterisks) without edema. A signal increase typically very anteriorly in the left sacrum (arrowheads) is a nonspecific finding [38]. **b** Supplementary semi-axial STIR MRI and semi-axial CT reconstructions display the right-sided accessory joint with surrounding bone marrow edema and sclerosis (arrows), respectively, and both iliosacral complexes (asterisk)

compartment had no added diagnostic value when evaluated on semi-coronal slices [104]. Cartilage sequences such as T1 fat-saturated or gradient-echo sequences may facilitate recognition of specific and clinically relevant erosion. Three cross-sectional studies (one of them controlled) using MRI volumetric interpolated breath-hold examination (VIBE) sequences reported superior sensitivity to detect erosion in the SIJ when compared to CT as gold standard, raising concerns that non-critical use of this sequence may overcall erosion by including also physiological or degenerative irregularities in SIJ morphology [105–107]. Furthermore, these reports did not demonstrate that VIBE sequences enhanced diagnostic

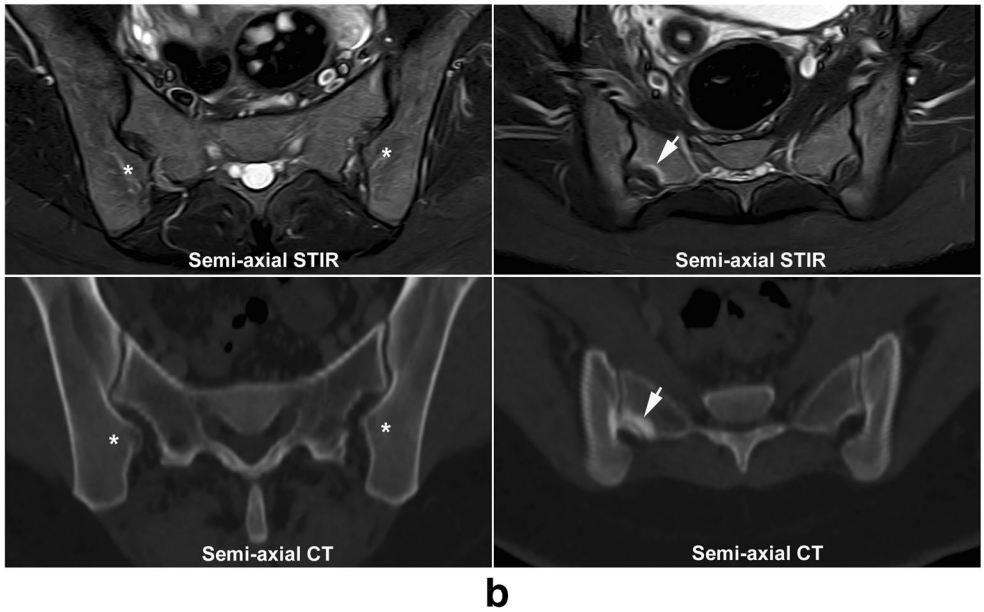

Fig. 4 (continued)

ascertainment. An uncontrolled pilot study exploring synthetic CT scans reconstructed by deep learning–based technology from multiple gradient-echo sequence MRI showed a numerically higher specificity with overlapping confidence intervals for detection of erosion versus standard T1SE sequence on SIJ quadrant level [108]. Larger samples are required to test whether this novel technique may improve diagnostic utility on patient level. Detection of SIJ erosion was enhanced by thinner MRI slice thickness of 2 or 3 mm [109]. There is no consensus about which segments of the spine should be scanned. MRI scans of the entire spine are usually obtained in the sagittal plane by T1-weighted and STIR sequences.

Is a Workstation Needed in Daily Practice?

Nowadays, many radiology departments offer referring physicians remote access to the imaging database inclusive of professional viewing software. The only extra expense for a rheumatology practice is a high-quality monitor, which can be acquired at affordable rates.

Training of Rheumatologists to Assess Axial MRI

Most rheumatologists have limited training in advanced imaging in SpA and thus rely on the reports by radiologists who may be more familiar with imaging features of degenerative than inflammatory back pain. According to a EULAR survey, training in MRI is included in the national curricula for rheumatologists in only 10% of countries, and competency is not assessed [93•]. Training courses in MRI are available in 29% of national rheumatology societies of EULAR countries suggesting that recent advances in the field cannot widely penetrate routine practice. One-day courses as well as online case-based content providing basic skills in MRI in SpA are offered by various organizations such as www.carearthritis.com or ASAS. However, we are not aware of an extended modular training program comparable to training in musculoskeletal ultrasound to refine skills by interactive sessions, discuss practice cases, and certify competency. Closing this gap of knowledge transfer by empowering rheumatologists to assess axial MRI by themselves is a prerequisite to disseminating advances in MRI in SpA into mainstream practice both in rheumatology and in radiology.

Standardized MRI Referrals and Reports

One of the common failures to appropriately assess imaging findings in axial SpA is a lack of shared terminology between radiologists and rheumatologists. Misunderstandings due to discrepant vocabulary and a limited dissemination of advances across both specialties result in deficient management of patients with axial SpA. Examples of mutual barriers were reported in both online surveys. Only 75% of UK senior radiologists were aware of the term of axial SpA published several years prior [91], while only 10% of EULAR rheumatologists were confident enough to assess axial MRI by themselves [93•]. A Canadian working group suggested a standard SIJ MRI reporting system by 4 categories: normal; alternate diagnosis; indeterminate findings not diagnostic for sacroiliitis; and sacroiliitis [110]. ASAS has launched an initiative to standardize the procedure of referral to and reports about imaging examination in axial SpA. On the background that imaging

can never diagnose axial SpA, but assist in the diagnostic pattern recognition, we recommend to routinely include an estimate of the probability whether axial SpA is present or not both in the referral letter by the rheumatologist and in the imaging report by the radiologist, assuming that the radiologist has been trained to perform this estimation. Another prerequisite to foster communication and collaboration between radiologists and rheumatologists are institutionalized meetings at local or regional level.

Future Directions

Projects for real-time recognition and quantification of SIJ BME by using computational neuronal networks are underway. Major challenges are the discrimination of BME from increased signal due to artifact or unrelated structures such as vessels, or the often still manual delineation of regions of interest. An essential limitation of techniques adopting artificial intelligence is their inability to retrace the contextual assessment of the complex lesion signature in axial SpA comprising both structural and active lesions. Provided computational neuronal networks can be better trained to discriminate true BME from other features displaying high signal intensity, artificial intelligence might assist in the future by a quick preliminary quantification of BME. However, the contextual assessment of the entire lesion spectrum in axial SpA remains the domain of human intelligence.

Conclusion

MRI alone cannot convey a diagnosis of axial SpA. In routine care, pattern recognition by synthesizing demographic, clinical, laboratory, and imaging findings epitomizes the diagnostic approach to axial SpA, a systemic inflammatory condition with high diversity in signs and symptoms. Limited utility of clinical and laboratory assessment for early recognition raised expectations whether advanced imaging may augment diagnostic confidence in clinically suspected early SpA. Contextual assessment of concomitant structural and active MRI lesions reflecting the whole spectrum of inflammation and bone remodeling in axial SpA is quintessential to enhance diagnostic utility in rheumatology practice. BME of moderate extent alone should not be regarded as diagnostic for axial SpA due to substantial background noise, which may result in inappropriate management. The role of pelvic radiographs as first imaging choice in suspected early SpA is debated. In health care settings providing low threshold access to advanced imaging, SIJ MRI is the preferred imaging modality in early axial SpA. Recent reports in the clinically challenging but data-deficient field of postpartum back pain suggest a wait period of 6–12 months after delivery before acquiring SIJ MRI, unless there is a high burden of symptoms suggestive of axial SpA. In most cases of clinically suspected axial SpA in daily routine, combined SIJ and spine MRI fitted into a standard MRI appointment should be acquired, in which spine MRI assists in differential diagnosis of alternate non-inflammatory back pain from diverse sources. Unmet needs to enhance the use of axial MRI in daily routine include uniform MRI protocols, standardized reporting of MRI findings, training modules how to evaluate axial MRI, and dissemination of imaging advances to the broad community of rheumatologists and radiologists.

Abbreviations ASAS, Assessment of SpondyloArthritis international Society; BME, bone marrow edema; BMI, body mass index; CRP, C-reactive protein; CT, computed tomography; HLA-B27, human leucocyte antigen B27; MRI, magnetic resonance imaging; SIJ, sacroiliac joint; STIR, short tau inversion recovery sequence; T1FS, T1 fat-saturated sequence; T1SE, T1 spin echo sequence

Declarations

Conflict of Interest The authors declare no competing interests.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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