Classification criteria in axial spondyloarthritis - what have we learned; where are we going?

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Key words

Axial spondyloarthritis; ankylosing spondylitis; classification; diagnosis; back pain; inflammation; magnetic resonance imaging; radiographs.

Key points

- Axial spondyloarthritis (axSpA) is a chronic inflammatory condition which can present with either radiographic changes or without.
- Historically there was the requirement for radiographic changes whereas the updated classifications incorporate clinical manifestations, family history, response to therapy, MRI, genetic and laboratory findings.
- Classification criteria have progressed in line with scientific advances incorporating the utility of MRI to identify inflammatory changes to the sacroiliac joint prior to radiographic changes.
- The ASAS classification criteria is the most relevant criteria set which increase the scope and parameters. They have facilitated SpA research including epidemiology, outcomes research and treatment.
- Clinical judgement remains the mainstay for diagnosis of axSpA. Physicians should not misuse classification criteria, avoiding their use before a clinical diagnosis is made.
- As time goes by, we are likely to see further refinement of classification criteria, especially as our understanding of genetics, biomarkers and immunopathophenotypes increases.

Synopsis/Abstract

Spondyloarthritis (SpA) is a chronic inflammatory condition which can have either a predominately peripheral or axial presentation. Axial SpA (axSpA) affects the axial skeleton with either radiographic or non-radiographic changes. The burden of radiographic axSpA (r-axSpA) and non-radiographic axSpA (nr-axSpA) is similar. However, radiographic changes are a late disease feature and earlier disease stages can be identified by incorporating other imaging methods, particularly MRI, or by combining clinical, laboratory and genetic findings, even in the absence of radiographic/MRI changes. The recognition of axSpA as a disease spectrum beyond ankylosing spondylitis (AS or r-axSpA) was considerably facilitated by the publication of the Assessment in Spondyloarthritis international Society (ASAS) classification criteria for axSpA. The diagnosis of axSpA is a clinical diagnosis and classification criteria are not aimed to be diagnostic tools**.** The split between r-axSpA and nr-axSpA is artificial and we should move towards the unifying concept of axSpA. Our understanding of genetics, biomarkers and immunopathophenotypes will drive further refinement of axSpA classification criteria.

Introduction

Spondyloarthritis (SpA) is a generic term for a family of diseases which can either have a predominantly axial (axial SpA [axSpA]; cardinal manifestation: chronic back pain) or a predominantly peripheral phenotype (peripheral SpA [pSpA]; cardinal manifestation(s): arthritis, enthesitis or dactylitis). The range of clinical features of SpA is broad and includes chronic (typically inflammatory) back pain, arthritis, enthesitis, dactylitis, as well as extra-articular manifestations (EAMs) such as psoriasis, uveitis and inflammatory bowel disease (IBD). SpA is associated with the major histocompatibility complex (MHC) class I human leucocyte antigen-B27 (HLA-B27)[1,2] and axSpA can be further divided into two subsets: axSpA with (radiographic axial SpA [r-axSpA] or ankylosing spondylitis [AS]) and without definite radiographic changes in the sacroiliac joints (non-radiographic axial SpA [nr-axSpA]).

SpA encompasses diseases historically designated as AS, psoriatic arthritis, enteropathic arthritis (IBD related arthritis), reactive arthritis, arthritis related to uveitis, and a sub-group of juvenile idiopathic arthritis (enthesitis-related arthritis [ERA]) (Figure 1). For this paper we will be focussing on the axial component of the disease. HLA-B27 is present in about 8% in populations of European descent and the prevalence of axSpA mirrors the prevalence of HLA-B27 in a given population, ranging between 0.3% and 1.4%.[3] The aim of this article is to highlight how diagnosis is evolving and classification of axSpA has changed, including much of the terminology.

Diagnosis and classification of axSpA

The diagnosis of axSpA should be a clinical exercise based on the recognition of a pattern of clinical, laboratory and imaging features that taken together are suggestive of axSpA. This exercise includes the consideration of differential diagnosis. Classification criteria are mainly used for research purposes and intended to create homogenous groups of patients with a certain condition applying a standardized definition. Figure 2 gives an historical perspective of SpA classification criteria over

time and landmark developments related to the development of new criteria; Table 1 summarises the various published criteria.

The modified New York (mNY) criteria for AS[2,4,5] required the presence of radiographic changes at the sacroiliac joint (SIJ)[6]. For a very long time, these were primary classification criteria for those patients suffering with IBP or with limitation of spinal/chest mobility[7]. The main limitation of these criteria is the requirement of definite radiographic changes of the SIJs; the criteria were often applied as diagnostic criteria and this has the very real potential of causing a delay to diagnosis and ultimately treatment. It is known that it can take several years prior to there being progression from inflammation in the SIJs to clear evidence of radiographic changes. Moreover a certain proportion of those with axSpA may never go onto develop definite radiographic damage and therefore, although unequivocally having the clinical characteristics of AS, may never fulfil these criteria.

Axial SpA: an historical perspective

The mNY criteria for AS[7] were published in 1985. It was a body of work that standardised the classification of AS; the change was to include sacroiliitis grade ≥2 bilaterally or sacroiliitis grade 3 unilaterally to define the presence of radiographic sacroiliitis; this was mandatory and clinical presentations alone were not enough. This could be potentially detrimental as radiographic changes may not always be present; moreover there is also the issue of discrepancies in interpretation of radiographs which can play a role in heterogeneity and further delay of diagnosis. The reliability of SIJ grading is poor, and training makes little impact on improving the reproducibility.[8] Equally the mNY clinical criteria do not take into account the peripheral and extra articular manifestations of the disease.

Following this the AMOR criteria were developed[9]. This however aims to classify patients within the entirety of the SpA group and is not specific to only the axial disease. Therefore for the purposes of classifying axSpA it helps but was not enough. This criterion uses a scoring system with more ≥6

being classifiable and ≥5 being probable of SpA. Adding a weighting structure is useful but can be seen as arduous. They utilise an imaging component but is only with a definite radiographic change (similar to the mNY criteria), which scores 3 points, the most attainable for a single component. The criterion then highlights a list of potential clinical components with associated scores being: lumbar or dorsal pain during the night, or morning stiffness of lumbar or dorsal spine (1 point); asymmetric oligoarthritis (2 points); buttock pain (1 point); if affecting alternately the right or left buttock (2 points); dactylitis (2 points); enthesitis (2 points); iritis (2 points); non-gonococcal urethritis or cervicitis accompanying, or within 1 month before, the onset of arthritis (1 point); presence or history of psoriasis, balanitis, or IBD (2 points); good response to NSAIDs in less than 48 hr, or relapse of the pain less than 48 hr if NSAIDs discontinued (2 points); presence of HLA-B27, of familial history of AS, Reiter syndrome, uveitis, psoriasis, or chronic enterocolopathies (2 points).

Then the European Spondyloarthropathy Study Group (ESSG) developed a criteria set. Their rationale was that there were areas of SpA which were being neglected in the classification which, ultimately, could help to better categorise patients belonging to the SpA spectrum. They completed a multi-centre Europe wide study identifying the sensitivity and specificity of a wider criteria set. They started with 183 variables but this was narrowed down to 25, then further to the following 7 with the primary criteria being that a patient had to have either IBP or synovitis (asymmetric or predominately lower limbs) and at least one of: positive family history; IBD; urethritis; cervicitis or acute diarrhoea ≤1 month before onset of symptoms; alternating buttock pain; enthesopathy; radiographic sacroiliitis. It is important to note that these criteria can be used for both axial and peripheral SpA and is not therefore specific to only axial disease. Sacroiliitis is dependent on radiographic changes but not inflammatory changes (only visible on MRI). This criteria does not include MRI inflammatory changes to the spine, nor radiographic for that matter, which could be perceived as a limiting factor. Nevertheless the sensitivity and specificity was comparable with the AMOR criteria with sensitivity 86.7% and 84.8% and specificity 87% and 89.9% respectively[10].

In 2009 the term axSpA was created by the Assessment of SpondyloArthritis International Society (ASAS) who went on to create the ASAS classification criteria for axSpA[11,12]. This is the first classification criteria developed after the introduction of MRI for axial disease[13]. Therefore one can assume that this concept would reduce the likelihood of their being false negatives on the basis of normal radiographic findings, it equally increased the positive predictive value of axSpA to 93.3%[14]. As there have been no further developments or new introductions of other criteria, from here on we will look into the use of this criteria set in more detail. It is important to emphasise again at this stage that classification criteria is not diagnostic, clinical reasoning can and should always supersede fitting patients into a particular classification structure[15]. The gold standard for diagnosis would still fall at the clinician to incorporate all the patient information including laboratory, imaging and clinical findings to complete the diagnosis[16].

The ASAS criteria have two arms from which a classification can be made, an imaging and a clinical arm. In the imaging arm, the presence of MRI inflammation, which plays an important role in the rheumatologist´s judgment to make a diagnosis of axial SpA, is a prominent factor, together with the classical presence of radiographic sacroiliitis. However, not all axSpA patients have sacroiliitis on imaging (for example, in the validation study of the ASAS criteria,[17] 25% of the patients did not have radiographic or MRI evidence of sacroiliitis), underscoring the fact that in clinical practice the rheumatologist bases his decision also on many other clinical and laboratory features, and that a diagnosis of axSpA can be made in the absence of sacroiliitis on imaging, including MRI sacroiliitis/inflammation.[18] The clinical arm was intended for use where there was no imaging available (or where imaging is negative)[19] and one therefore cannot assume or prove radiographic or inflammatory changes of the sacroiliac joints. Because of the strong association of sacroiliitis with axSpA, and because of high sensitivity and specificity, if sacroiliitis on imaging is present, only 1 other SpA feature needs to be present to classify a patient as having axSpA according to the ASAS criteria, while 2 additional features are required in the HLA-B27/clinical arm.[17] The features and requirements of each arm are listed in Table 1.

The new criteria for axSpA can be applied in patients with back pain for longer than 3 months with an onset before the age of 45 years.[11,12] Of note, chronic back pain, not necessarily being IBP, is present as an entry criterion, reflecting the fact that in clinical practice, patients with non-inflammatory chronic back pain may represent up to 20-30% of patients with axSpA, while IBP can be observed in 20-25% of patients with non-inflammatory (mechanical) causes of chronic back pain.[20-22] Detailed analysis in the ASAS axSpA validation study also demonstrated that IBP as an entry criterion did not perform better than chronic back pain.[17] However, the presence of IBP is an important symptom that should prompt further diagnostic tests for axSpA. Age is also an important factor in the entry criteria, reflecting the fact that complaints associated with axSpA usually start in the second or third decade of life, and by the age of 45 years, more than 95% of patients are symptomatic.[23] Importantly, evidence suggests that disease activity, comorbidities and treatment responses are similar for nr-axSpA and r-axSpA.[24]

A critical view of the components of the ASAS classification criteria for axSpA

Under the imaging arm it is first prudent to consider the aspects of positivity. The primary issue being a low inter and intra rater reliability of radiograph interpretation.[25] Within the skein of MRI interpretation it is important to consider the impact of mechanical elements on an interpretation of sacroiliitis suggestive of axSpA. Bone marrow oedema (BMO)/osteitis is not unique to inflammatory conditions, it has been shown to be present in post-partum women (with and without pelvic pain), cleaning staff, long distance runners, soldiers, athletes and healthy individuals[26-29]. However, differences in the level of BMO of the axSpA group compared to the mechanical group have been reported, with axSpA having a tendency to higher levels of inflammation and presence of erosions, ankylosis and fat infiltration. The mis-interpretation of inflammation has been explored further with extensive and intermediate inflammation having a higher odds ratio of developing erosions at the SIJ after 4 years[30], leading to the conclusion that limited BMO may be due to transient mechanical force

but extensive BMO appears to have a higher correlation to pathological changes. With extensive changes having more than 1 cm depth of inflammation.

The performance of MRI in the diagnosis of axSpA was recently systematically reviewed by Jones et al.[31] The authors found that, at the SIJ level, BMO is the most sensitive and specific individual lesion. Structural lesions including fat deposition have moderate sensitivity and specificity, whilst erosions demonstrate good specificity but relatively poor sensitivity (with the caveat that some of the studies used high fixed specify values, which may have add a negative impact on sensitivity values). Combination of BMO and erosions, or BMO and fat deposition, yielded higher sensitivity and specificity than BMO alone. Pre-defined numbers of lesions or cut-offs have also been analysed and suggest that BMO in ≥3 quadrants and erosions in ≥3 quadrants show high sensitivity and specificity and presence of 3-5 fatty lesions also yield good sensitivity. However, further studies are required to validate these findings. In the spine, studies investigating the value of corner inflammatory lesions found moderate sensitivity and specificity, whilst spinal fatty lesions were found to have relatively poor sensitivity and specificity. Although the results suggest that spinal lesions alone are unlikely to have sufficient diagnostic performance for use in axSpA, these lesions might be useful in combination with features identified on SIJ MRI (an area that requires further research).

The systematic literature review by Jones et al.[31] served as evidence to support recommendations for acquisition and interpretation of MRI of the spine and sacroiliac joints in the assessment of patients with suspected axSpA,[32] including recommended sequences, anatomical coverage, acquisition parameters and interpretation of active and structural MRI lesions. The full list of recommendations can be found in the article but two key messages should be highlighted: 1) imaging cannot be viewed in isolation and needs to be interpreted in the context of clinical presentation and results of laboratory investigations, and 2) 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 (i.e. contextual interpretation of active and structural lesions is key to enhancing diagnostic utility of MRI is patients with suspected axSpA).

HLA-B27 positivity is given a high level of weighting in the classification of axSpA according to ASAS, however due to it requiring two SpA features and imaging only requiring one feature it leads to imaging taking precedence. This is further reflected as there is also an increased prevalence of HLA-B27 in the r-axSpA group over nr-axSpA[33,34]. HLA-B27 is positive in 85-95% of r-axSpA patients and in 75-85% of nr-axSpA patients.[35-37]

One classification feature of SpA is a positive family history of the disease. The question here is what is the relevance? If we have further information already, such as HLA-B27 status, does a family history assist our diagnosis further? Which SpA feature is more relevant to a diagnosis of axSpA? Van Lunteren and colleagues[38] looked at three cohorts of axSpA patients to identify if a family history was relevant if the HLA-B27 status was known. They found that there was no consensus across all three groups. A family history of AS was relevant in the ASAS cohort but not in the *DEvenir des Spondyloarthropathies Indifferenciees Recentes* (DESIR [a longitudinal French cohort including patients aged 18-50 with IBP])[39] or the European SPondyloArthritis Caught Early (SPACE [an inception cohort including patients aged ≥16 years old with chronic back pain from the Netherlands, Italy, Norway or Sweden])[40] cohorts; equally family history of acute anterior uveitis was associated with a diagnosis in the SPACE cohort but not the ASAS or DESIR groups. This indicates that HLA-B27 has a greater relation to a positive diagnosis of axSpA than a positive family history does.

Further work into a positive family history has tried to identify which diagnosis in the SpA family has a greater probability of association with axSpA[16]. A positive correlation was seen between a family history of AS or anterior uveitis, when correlated with HLA-B27 status. Reactive arthritis, IBD or psoriasis did not contribute to a diagnosis of axSpA. Therefore while considering family history as a positive SpA feature to cement the patient's diagnosis, it would appear there is a hierarchy to consider. There also appears to be some evidence that utilising HLA-B27 status, if known, is more useful[16].

An elevated CRP is an important component. CRP can be elevated in up to 40 percent of patients with axSpA, and is more frequently elevated in patient with r-axSpA than in patients with nr-axSpA.[41] Therefore, its sensitivity in axSpA can, and has been questioned[35]. However a positive CRP is one of the associated risk factors for developing radiographic progression[6]. CRP is also a component of the Ankylosing Spondylitis Disease Activity Score (ASDAS), a composite measure of disease activity.[42-44] On the basis that there is less positivity in nr-axSpA than r-axSpA and a higher distribution of females in the nr-axSpA group than r-axSpA group[19], is this a case where females with the disease tend to have lower CRP's than males? If so it raises the question, when incorporating CRP in the classification criteria that there will be a higher CRP in the r-axSpA group than the nr-axSpA group.

Dactylitis is a component which can increase the susceptibility of axSpA and can occur as a peripheral manifestation. The ESPeranza cohort, a cohort of patients from Spain, assessed the frequency of dactylitis within the SpA group and found an incidence of 9.5%[45]. This is slightly higher than those found in the SPACE cohort[40]. Although dactylitis is associated with peripheral SpA it has been identified that 15% of all patients who had a diagnosis of dactylitis had axial and not peripheral SpA.[45]

Enthesitis is another peripheral manifestation that has been highlighted as an aspect contributing to classification; it is one, which in the clinic, is a straightforward component to assess. The ASAS classification criteria only include enthesitis in the heel with their criteria, and do not include others; this has been further supported with work by Ozsoy-Unubol and Yagci[46] who completed ultrasound assessments on 9 enthesitis points in a range of patients with axSpA and mechanical back pain. Their assessment was of Achilles; plantar fascia; patella tendon, distal and proximal; quadriceps; tibialis anterior; triceps; common flexor tendon and the common extensor tendon. They identified that the most common site for power Doppler signal and calcification (a finding with diagnostic value[47]) was the Achilles and patella tendon, with actually the distal and proximal patella tendon having the highest incidence in the axSpA group. The issue however, is that these patellar areas were also the highest incidences in the mechanical back pain group; whereas enthesitis of the Achilles was

prevalent in 40% of the axSpA group but was only present in 6.7% of the mechanical back pain group. This highlights a number of things; primarily that enthesitis can be inflammatory or mechanical, therefore enthesitis in isolation should be viewed with caution as this could be a mechanical cause from changes in activity or exercise loads, and that enthesitis at the patella, as long as not mechanical can add significance to the diagnosis of axSpA.

The other issue is one of concomitant fibromyalgia. Areas of enthesitis that are assessed in axSpA are similar to the pain point areas assessed when considering a diagnosis of fibromyalgia[48]; therefore multiple positive 'enthesitis' sites on a patient should be assessed with caution for what could be an underlying fibromyalgia which can have similarities to the presentation of axSpA[49-52]. The use of ultrasonography for assessment of enthesitis may reduce the number of false positives of clinical identification of pain without pathology in the tendon[53]. However, it is recognised that not every facility will have access to an ultrasound assessment in clinic and instead will need to wait for a radiology review, all of which could further delay the diagnostic work up.

Uveitis is also a SpA feature, in this case an EAM; up to 33% of axSpA patients will develop uveitis[54], 50% of those who have suffered with uveitis will go onto develop recurrent disease[55]. Uveitis can be classified as infectious, non-infectious (associated with axSpA) or masquerade[56]. The standardisation of uveitis is then descriptive of anatomical location being anterior, intermediate, posterior or panuveitis[57]. It has been shown that 85% of uveitis in SpA patients will be anterior[58]. The other aspects to uveitis which make it so useful to assist with classification is that the age of onset is between 20 and 59 years[59], although this is higher than that for axSpA it is similar and therefore one could assume that they can go together at both diagnosis and within the clinical follow up setting. Interestingly HLA-B27 positive uveitis presents as a non-granulomatous acute anterior uveitis (AAU)[60], this has led to the development of studies to identify those patients with AAU and HLA-B27 positivity to try and identify if they have an underlying axSpA[61].

There is a close association between SpA and IBD. There is a growing body of evidence which suggest that the IBD profile and that of SpA is in fact one and the same[62-64]. The reason for this could be that the gut is the primary interaction site between the host immune system and micro-organisms[63]. The 'trigger' of axSpA could be that following inflammation in the gut there is a change to the adaptive immune system and the new 'normal' of antibody status has changed from previously therefore triggering an autoimmune response[65]. Both diseases also share the HLA-B27 antigen which is why 6.5% of SpA patients will develop IBD within 5 years from diagnosis, and 30% of IBD patients will develop a SpA[65]. In addition synovial T cells could be developed from the gut as there have been found to be the same macrophages in the gut as in the synovium[64]. Clearly these two conditions overlap a great deal and should each be taken into consideration when diagnosing and managing the other, particularly since 46.2% of SpA patients without bowel symptoms or disease had inflammation in the bowel on colonoscopy[66].

The link between psoriasis and the SpA spectrum is clear[67]. The question is the relevance of psoriasis in axial disease. Is it a different pathology to psoriatic spondylitis? Being axSpA, is the axial involvement one of the manifestations of a peripheral disease? There is currently no widely accepted definition of axial involvement in psoriatic arthritis (PsA). Since there might be differences in efficacy of certain drugs/mechanisms of action for peripheral and axial manifestations of the disease, ASAS and the Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) have agreed to develop a consensus definition of axial involvement in PsA to be used for research purposes. Such a definition will serve primarily as a classification tool to be applied to patients with clinically diagnosed PsA in order to build a homogeneous group of patients for inclusion in non-interventional or interventional studies.

The CLassification of Axial SpondyloarthritiS Inception Cohort (CLASSIC) study

In October 2013, after a two-day meeting of the Arthritis Advisory Committee (AAC), a panel of experts who make recommendations to the FDA, the FDA rejected the application by two manufacturers of TNF-blockers (adalimumab and certolizumab) for the treatment of nr-axSpA. One of the reasons was concern from the FDA regarding the specificity of the ASAS axSpA classification criteria when erroneously used for diagnostic purposes. This has led to a delay in US regulatory approval for nr-axSpA compared to the EMA (first EMA approval in 2012; first FDA approval in 2019, following the conduct of new phase 3 clinical trials for nr-axSpA recommended by the FDA).

In 2017, a meta-analysis showed that the ASAS axSpA criteria performed well in patients included in seven cohorts from various geographic areas.[68] The meta-analysis included 4990 patients in total, generating a very high pooled sensitivity and specificity (82% and 87% respectively) for the axSpA criteria, with little variation across studies. The pooled sensitivity of the imaging arm (± clinical arm) and clinical arm (± imaging arm) was 57% and 49%, respectively (26% and 23% when considering patients fulfilling each arm exclusively). High estimates of pooled specificity were found for both arms, irrespective of the definition (range: 92%–97%). However, the LR+ of the imaging arm only was higher as compared with the clinical arm only (9.6 vs 3.6). It should be noted that the criteria's performance also depends on the prevalence of SpA in the underlying population (pre-test probability).

Despite these results, the validity of the ASAS axSpA criteria has been questioned. Hence, there has been the development of the CLASSIC study (NCT03993847). This is aimed at identifying the current sensitivity and specificity of the classification criteria worldwide. This longitudinal study is aiming to recruit 500 patients from North America (a minimum of 300 from the United States) and 500 from outside North America. It is an inception cohort wherein those patients referred to rheumatology with undiagnosed back pain of ≥3 months duration with onset ≤45 years of age will be recruited. The primary objective of the trial is to validate the performance of the current ASAS classification

criteria; if a specificity of ≥90% and a sensitivity of ≥75% of the original ASAS criteria will be found in the study, the ASAS criteria will be considered validated and no further analyses will be done. Only if the primary objective is not met, refinements of the criteria will be made and tested. A secondary objective is to identify confidence in ascertainment of (active) sacroiliitis by MRI. The tertiary outcome is to determine the predictive value of the criteria over a 5 year follow up period.

Conclusion

This review has aimed to highlight issues about the diagnosis and classification of axSpA, namely the issue of over diagnosis; how mechanical factors can play a large role in altered imaging on MRI which could alter the outcome of the imaging arm. In addition we have highlighted that caution should be used when considering certain components of the criteria to classify the disease, especially under the clinical arm. For example, although clearly enthesitis has its place and when used appropriately it can alter the clinician's decision, it has been shown that the exact weighting of this should be carefully considered.

We are working in a time when medical advances mean that both assessment and treatment are continually progressing. If one treatment is not efficacious there are a wider range of alternative treatment options and less barriers, as these become more financially competitive. Therefore we must be clear, that the correct diagnosis has been made and that we, as clinicians, are not 'jumping' to an incorrect diagnosis through poorly understood or mis-interpreted findings as diagnostics. This is a time to be excited, but also cautious with the progress in identifying and diagnosing, this complex and often missed spectrum of diseases, particularly in a time where there are more Allied Health Professionals (AHP's) working in primary and secondary care and will be instrumental in the diagnosis of such conditions.

The future in this condition should work to further educate health care providers about SpA and their features, and how the specificity of imaging can impact diagnosis and what role EAMs play in

this. The diagnosis of axSpA is a clinical diagnosis and classification criteria are not aimed to be diagnostic tools**.** The split between r-axSpA and nr-axSpA is artificial and we should move towards the unifying concept of axSpA. Our understanding of genetics, biomarkers and immunopathophenotypes will drive further refinement of axSpA classification criteria.

It is important we diagnose this potentially disabling condition early. What should be developed is a way to stratify these patients into the correct diagnosis. That could, and should include further identification of the susceptibility of the condition within the broader hospital setting and those clinicians assessing and diagnosing those patient with the SpA features, such as dermatology, gastroenterology, ophthalmology to have a lower threshold for referring their patients for an opinion from rheumatology if they present with chronic spinal/buttock pain. Equally in primary care more attention should be sought to identify those patients with other clinical manifestations and raising awareness to their care providers; whether this be General Practitioners or the ever growing and developing role of AHP's fulfilling these roles in the community.

TABLES

Table 1. Published classification criteria for spondyloarthritis*

mNY criteria for AS	**Entry criterion:**	Imaging criterion plus ≥1 clinical criterion		**Imaging criterion:**	Radiographic sacroiliitis†	**Clinical criteria:**	• Low back pain and stiffness for more than 3 months that improves with exercise, but is not relieved by rest • Limitation of motion of the lumbar spine in the sagittal and frontal planes • Limitation of chest expansion relative to normal values correlated for age and sex
Amor criteria for SpA		Sum of points of items below must be ≥6; a sum of points ≥5 classifies for probable SpA			Radiographic sacroiliitis† (3 points)		• Lumbar or dorsal pain during the night, or morning stiffness of lumbar or dorsal spine (1 point) • Asymmetric oligoarthritis (2 points) • Buttock pain (1 point), if affecting alternately the right or the left buttock (2 points) • Dactylitis (2 points) • Enthesitis (2 points) • Iritis (2 points) • Non-gonococcal urethritis or cervicitis accompanying, or within 1 month before, the onset of arthritis (1 point) • Acute diarrhoea accompanying, or within 1 month before, the onset of arthritis (1 point) • Presence or history of psoriasis, balanitis, or IBD (Crohn's/ulcerative colitis) (2 points) • Good response to NSAIDs in less than 48h, or relapse of the pain in less than 48h if NSAIDs discontinued (2 points) • Presence of HLA-B27, or familial history of AS, Reiter syndrome, uveitis, psoriasis, or chronic enterocolopathies (2 points)
ESSG criteria for SpA		IBP (modified Calin)[21] or synovitis (asymmetric or predominantly in the lower limbs), and ≥1 clinical or radiological criterion			Radiographic sacroiliitis†		• Buttock pain alternating between right and left gluteal areas • Urethritis, cervicitis, or acute diarrhoea within one month before arthritis • Inflammatory bowel disease • Psoriasis • Positive family history
ASAS criteria for axSpA		CBP (≥3 months) with an onset <45 years of age and:	a) Imaging criterion plus ≥1 the clinical	b) Positive HLA-B27 plus ≥2 other	Radiographic sacroiliitis† or MRI sacroiliitis‡		• IBP (ASAS)[69] • Arthritis • Enthesitis (heel) • Uveitis • Dactylitis

			criteria or	clinical criteria				• Psoriasis • Crohn's/ ulcerative colitis • Elevated CRP • Good response to NSAIDs • Family history of SpA • HLA-B27
ASAS criteria for pSpA		Peripheral arthritis, enthesitis or dactylitis and:	a) Imaging criterion or ≥1 clinical SpA feature from group A or	b) ≥ 2 other clinical SpA features from group B		Radiographic sacroiliitis† or MRI sacroiliitis‡		**Group A** • Uveitis • Psoriasis • Crohn's/ulcerative colitis • Preceding infection • HLA-B27 **Group B** • Arthritis • Enthesitis • Dactylitis • IBP ever (ASAS)[69] • Family history for SpA
*Please note that the definition of IBP and some SpA features varies between different criteria sets; for details please consult the original publications. †Defined as radiographic sacroiliitis grade ≥2 bilaterally or grade 3-4 unilaterally: grade 0 = normal; grade 1 = suspicious changes; grade 2 = minimum abnormality (small localized areas with erosion or sclerosis, without alteration in the joint width); grade 3 = unequivocal abnormality (moderate or advanced sacroiliitis with erosions, evidence of sclerosis, widening, narrowing, or partial ankylosis; grade 4 = severe abnormality (total ankylosis). ‡Defined as bone marrow oedema (short tau inversion recovery sequence) or osteitis (T1 post-gadolinium sequence) highly suggestive of SpA, clearly present and located in the typical anatomical areas (subchondral or periarticular bone marrow); if there is only one signal (lesion) per MRI slice suggesting active inflammation, the lesion should be present on at least two consecutive slices; if there is more than one signal (lesion) on a single slice, one slice may be sufficient. Abbreviations: AS, ankylosing spondylitis; ASAS, assessment of spondyloarthritis international society; axSpA, axial spondyloarthritis; CBP, chronic back pain; CRP, C-reactive protein; ESSG, European spondyloarthropathy study group; HLA, human leukocyte antigen; IBD, inflammatory bowel disease; IBP, inflammatory back pain; mNY, modified New York; MRI, magnetic resonance imaging; NSAIDs, non-steroidal anti-inflammatory drugs; pSpA, peripheral spondyloarthritis; SpA, spondyloarthritis.								

FIGURES

Figure 1. The spondyloarthritis spectrum. IBD, inflammatory bowel disease; U-SpA, undifferentiated spondyloarthritis.

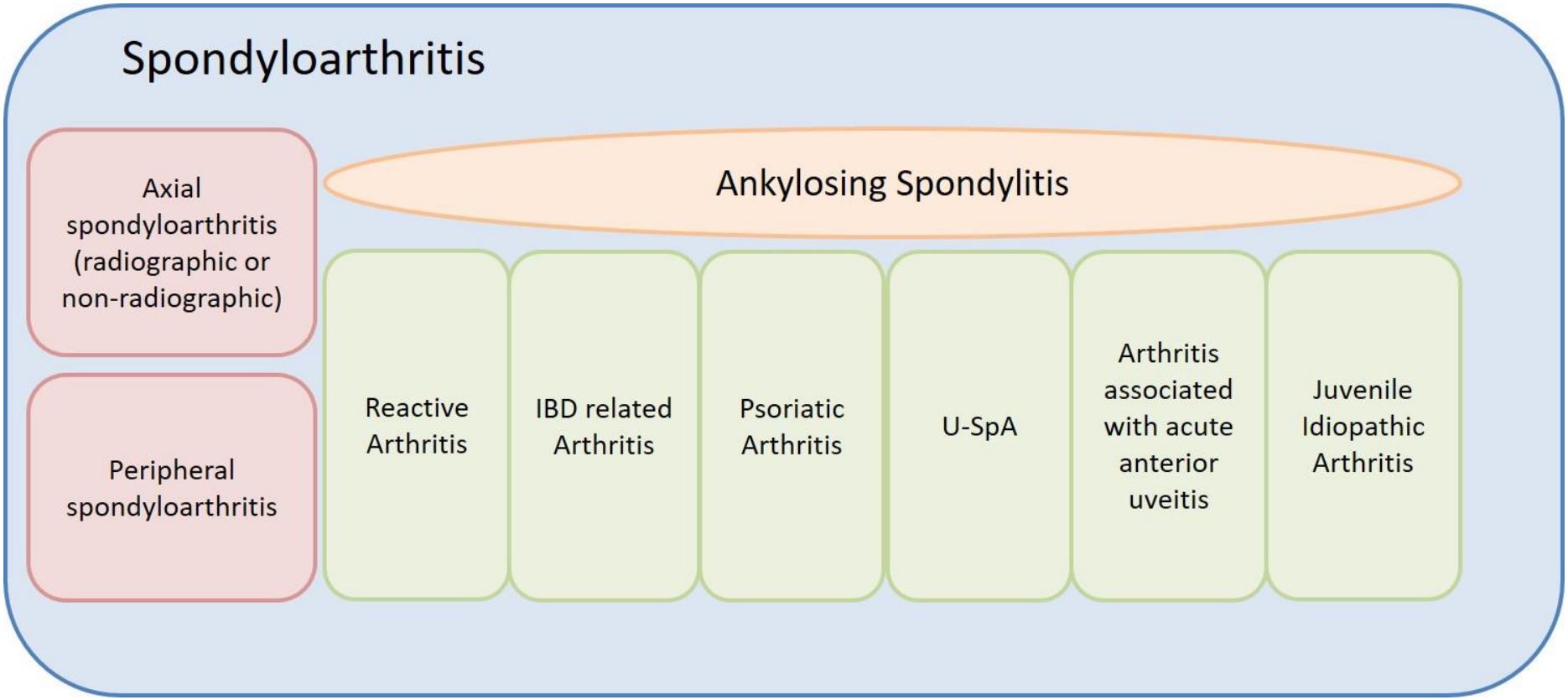
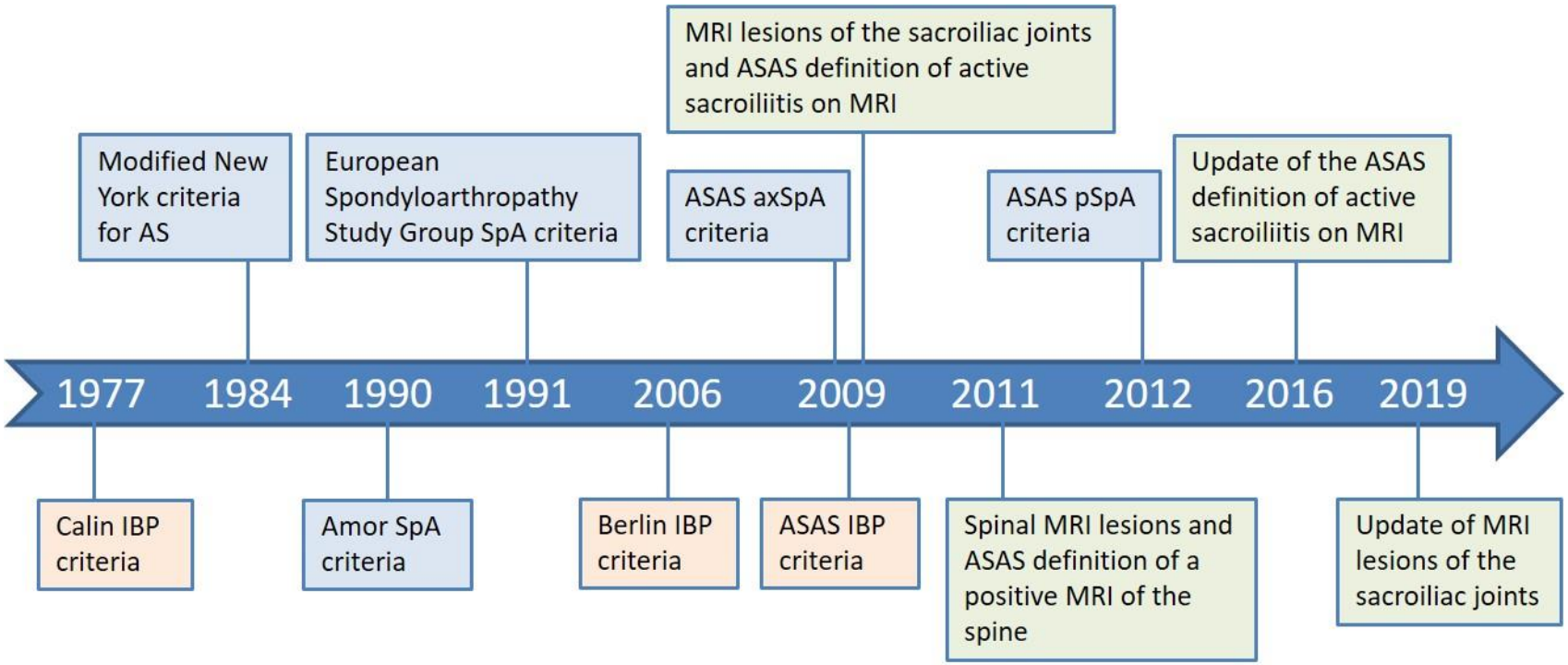


Figure 2. Development of classification criteria for spondyloarthritis and inflammatory back pain and MRI definitions over time. AS, ankylosing spondylitis; ASAS, Assessment of Spondyloarthritis international Society; axSpA, axial spondyloarthritis; IBP, inflammatory back pain; MRI, magnetic resonance imaging; pSpA, peripheral spondyloarthritis; SpA, spondyloarthritis.[7,9,10,12,20,21,69-74]



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