REVIEW ARTICLE

How should we diagnose spondyloarthritis according to the ASAS classification criteria

A guide for practicing physicians

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KEY WORDS

ankylosing spondylitis, axial and peripheral spondyloarthritis, classification criteria, magnetic resonance imaging

ABSTRACT

The Assessment of SpondyloArthritis International Society (ASAS) group has recently developed criteria to cla ssify patients with axial SpA with or without radiographic sacroiliitis, and criteria to classify patients with peripheral SpA.

The ASAS axial criteria consist of 2 arms and can be applied in patients with back pain (>3 months almost every day). In one arm, imaging (radiographs and magnetic resonance imaging [MRI]) has an important role, in the other arm – HLA-B27. MRI can detect active inflammation and structural damage associated with SpA. According to the ASAS axial SpA criteria, patients with chronic back pain aged less than 45 years at onset can be classified as having axial SpA if sacroiliitis on imaging (radiographs or MRI) plus 1 further SpA feature are present, or if HLA-B27 plus 2 further SpA features are present.

The ASAS peripheral criteria can be applied in patients with peripheral arthritis (usually asymmetric arthritis predominantly involving the lower limbs), enthesitis, or dactylitis. Patients can be classified as having peripheral SpA if 1 of the following features is present: uveitis, HLA-B27, preceding genitourinary or gastrointestinal infection, psoriasis, inflammatory bowel disease, sacroiliitis on imaging (radiographs or MRI), or if 2 of the following features besides the entry feature are present: arthritis, enthesitis, dactylitis, inflammatory back pain, or a positive family history of SpA.

The ASAS criteria for axial and peripheral spondyloarthritis Traditionally, spondyloarthritis (SpA) is subdivided into subtypes consisting of ankylosing spondylitis (AS), arthritis associated with inflammatory bowel disease (IBD), arthritis associated with acute anterior uveitis, reactive arthritis, and undifferentiated SpA (uSpA) (FIGURE 1). Patients with typical features of SpA who cannot be assigned to any of the specific SpA subgroups, can be classified as having uSpA.[1,2] According to some definitions, also juvenile SpA and psoriatic arthritis can be included in the SpA group.[2,3] Some authors identify arthritis associated with psoriasis as an SpA subgroup, while others recognize it as a distinct disease.[2,4] A distinction is typically made between patients with a symmetric, polyarticular pattern and patients with arthritis of the SpA type, which has asymmetric, oligoarticular arthritis character involving the lower limbs. The first group of patients can be recognized as having a distinct disease, while the second group can be considered as an SpA subgroup.[2]

To classify patients with SpA, various criteria sets can be used. The oldest are the Amor criteria and the European Spondyloarthropathy Study Group (ESSG) criteria. They were both developed in the 1990s (before magnetic resonance imaging [MRI] was available) and addressed all SpA subtypes.[5] The ESSG criteria have inflammatory back pain (IBP) and peripheral arthritis as entry criteria, while the Amor criteria do not have any entry criteria. The latter consist of a list of signs, none of which is required to classify a patient as having SpA. According to the ESSG criteria, patients with at least 1 of the entry criteria

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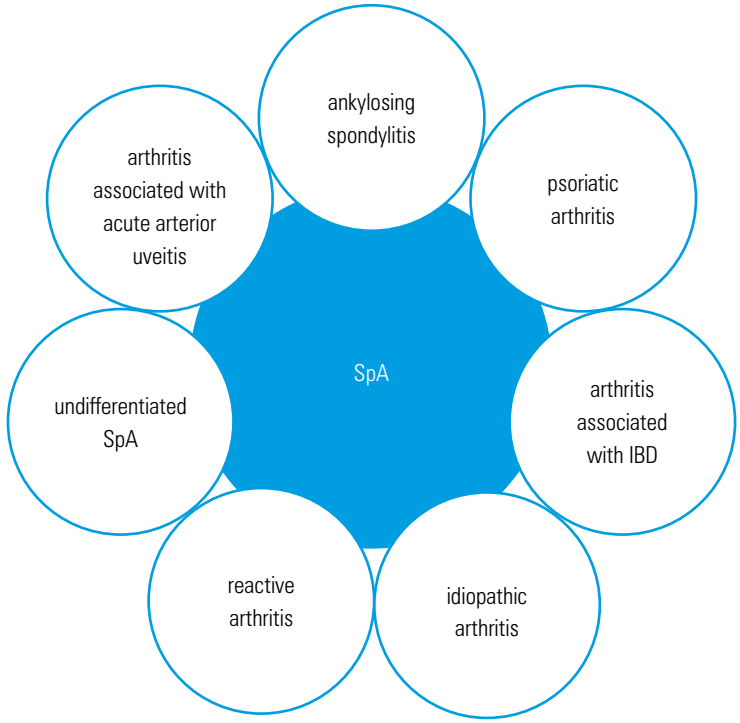

FIGURE 1 The concept of spondyloarthritis
Abbreviations: IBD – inflammatory bowel disease, SpA – spondyloarthritis

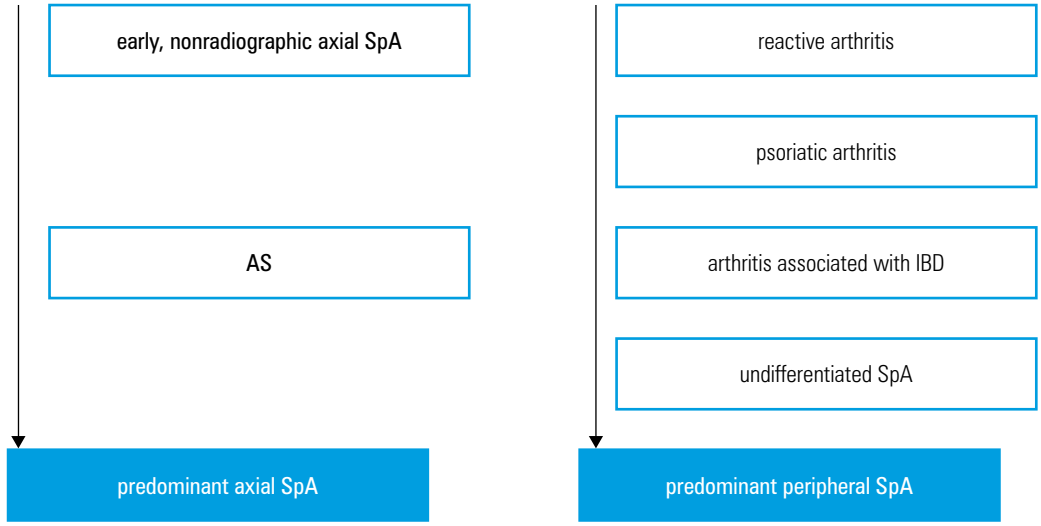

FIGURE 2 Predominant axial and predominant peripheral spondyloarthritis
Abbreviations: AS – ankylosing spondylitis, others – see FIGURE 1

and 1 minor criterion are classified as having SpA.[2,6-9]

Recently, it has been proposed to divide SpA patients into subgroups according to clinical presentation (FIGURE 2). The Assessment of SpondyloArthritis International Society (ASAS) group has developed criteria to classify patients with axial SpA with or without radiographic sacroiliitis, and criteria to classify patients with predominant peripheral SpA.[3,5] In the axial subtype of SpA, complaints of the back are the most dominant feature (FIGURE 3), while in the second subtype, peripheral arthritis, dactylitis, or enthesitis is the most dominant feature (FIGURE 4). However, in both diagnoses all other features can be present.[1]

Ankylosing spondylitis and axial spondyloarthritis: one disease or separate entities? Besides the criteria sets to classify patients with axial SpA, there are criteria to classify patients with AS, namely the modified New York criteria.[10] An essential part of these criteria is the presence of radiographic sacroiliitis because it is frequently observed in patients with AS.[3,5] In more than 90% of patients with AS, radiographic sacroiliitis is present.[3] According to the modified New York criteria, a patient is classified as having definite AS if 1 clinical criterion together with a radiological criterion are present.[10] Complaints associated with AS usually start in the 3rd decade of life, and by the age of 45 years, more than 95% of patients are symptomatic. Most of them suffer from back pain resulting from inflammation in the sacroiliac (SI) joints and/or spine, which can lead to structural damage over time.[2,3]

Generally, inflammation starts in the SI joints, and it often takes 6 to 8 years before radiographic sacroiliitis is detectable on plain radiographs.[1,11,12] However, the underlying mechanisms of the inflammatory process leading to new

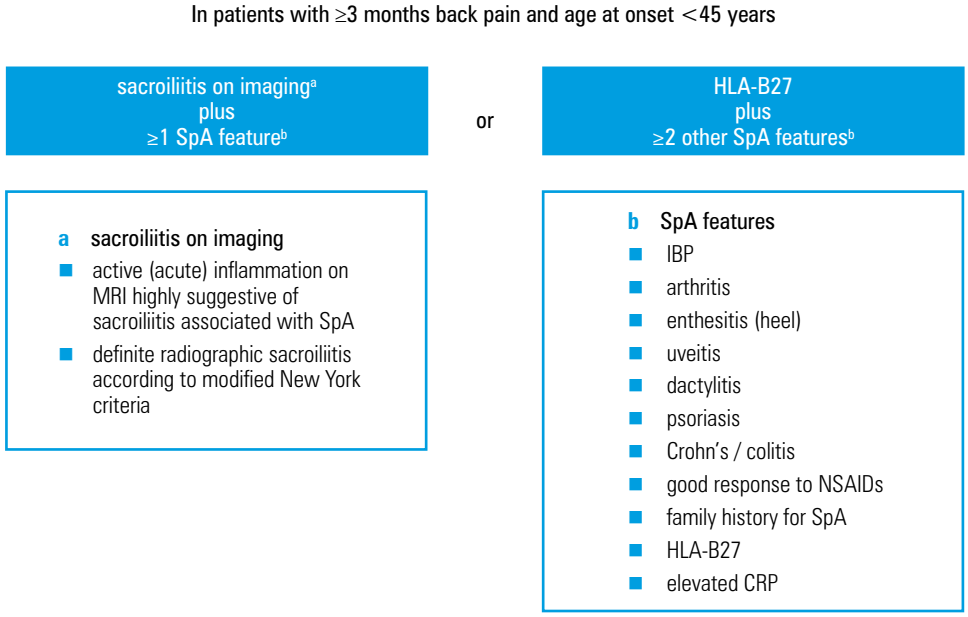

FIGURE 3 ASAS axial spondyloarthritis criteria Abbreviations: CRP – C-reactive protein, IBP – inflammatory back pain, MRI – magnetic resonance imaging, NSAID – nonsteroidal anti-inflammatory drug, others – see FIGURE 1

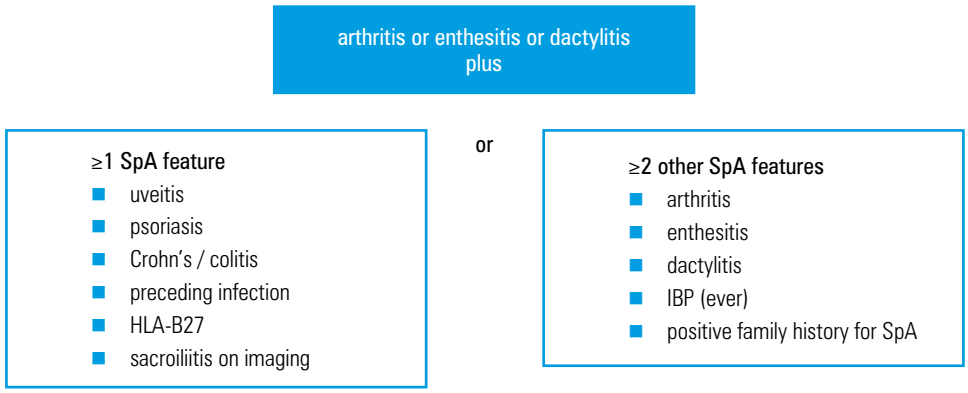

FIGURE 4 ASAS peripheral spondyloarthriris criteria Abbreviations: see FIGURES 1 and 3

bone formation are not fully understood.[2,13] It is thought that radiographic changes reflect the consequences of inflammation rather than inflammation itself.[1,11,12] Thus, the occurrence of radiographic sacroiliitis in patients with axial SpA is mainly a function of time, with some influence of severity factors. Besides, patients with nonradiographic axial SpA have the same high disease activity as patients with established AS in terms of signs and symptoms.[14] Therefore, patients with nonradiographic axial SpA and patients with established AS reflect different stages of a single disease continuum and, thus, the same disease entity (FIGURE 5).[11]

What's new? The new ASAS criteria for axial SpA can help identify patients with axial SpA but without radiographic sacroiliitis. Before the ASAS axial criteria were available, only patients with radiographic sacroiliitis could be classified according to the modified New York criteria, or the whole group of SpA was addressed by the ESSG and Amor criteria. With the new ASAS criteria, 2 separate classification criteria sets exist for the predominantly axial SpA and predominantly peripheral SpA.

The new criteria for axial SpA can be applied in patients with back pain for longer than 3 months and the onset before the age of 45 years. Age is an important factor in the entry criteria of the ASAS axial SpA criteria, while the character of the back pain is not. The latter was important in the ESSG criteria as entry criteria. However, based on literature review, the probability that a patient with IBP has SpA increases only to 14% compared with 5% probability of SpA in all patients with chronic back pain, so it is not considered useful as an entry criterion in the ASAS axial SpA criteria.[2] Moreover, during the development process, the performance of the criteria with IBP as mandatory was compared with having back pain as an entry criterion. In the validation set, many patients having SpA according to rheumatologists did not have IBP, and vice versa, many patients with IBP did not have SpA. Consequently, the criteria with IBP as a mandatory symptom did not perform better. Meanwhile, the combination of IBP with other SpA features can increase the probability of SpA, and therefore IBP still has a role in the ASAS axial and peripheral SpA criteria, but as one of the SpA features instead of being an entry criterion. The ASAS peripheral SpA

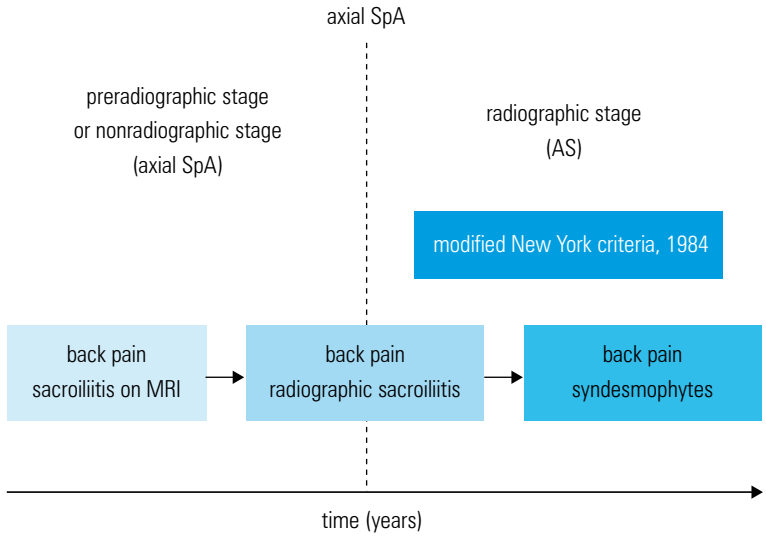

FIGURE 5 The concept of axial spondyloarthritis; patients with and without radiographic sacroiliitis
Abbreviations: see **FIGURES 1, 2,** and **3**

criteria can be applied in patients with peripheral arthritis, enthesitis, or dactylitis.

Another important new feature of the ASAS axial SpA criteria is that they consist of 2 arms. In one arm, MRI has an important role, and in the other – HLA-B27. HLA-B27 status is a relevant tool that allows to distinguish SpA from no SpA, since it is strongly associated with SpA.[2,6] Of the patients with uSpA, 70% is HLA-B27--positive, while this association is even stronger with AS according to the modified New York criteria (80%–95% HLA-B27-positive). In the general population, only 5% to 10% is HLA-B27--positive.

Nonetheless, HLA-B27 testing is not useful as a single diagnostic tool in patients with chronic low back pain without further SpA features, because the post-test probability in this population is 30% at best. Other clinical and imaging features should also be used to make a diagnosis.[6] Therefore, apart from HLA-B27 positivity, 2 other SpA features need to be present to classify a patient as having axial SpA.

MRI is important in the other arm, since it has become the most suitable method of detecting inflammation associated with SpA. MRI helps detect active inflammation and structural damage. Active inflammatory lesions are best visualized by fat-saturated T_2-weighted turbo spin-echo sequence or a short tau inversion recovery (STIR) sequence, while chronic lesions are best visualized by T_1-weighted turbo spin-echo sequence.[15] There is no appropriate gold standard available to test sensitivity, but it is estimated at about 90%. Specificity is also estimated at about 90%,[9,11] but can be higher if MRI is performed and interpreted correctly.[2,3] Because of the strong association of sacroiliitis with axial SpA, and because of high sensitivity and specificity, only 1 other SpA feature needs to be present to classify a patient as having axial SpA.

Active sacroiliitis on MRI can predict future appearance of sacroiliitis on radiographs.[12] Therefore, it is important to identify inflammation of the SI joints on MRI in early axial SpA.[2,3] A substantial proportion of patients with active inflammation on MRI will develop structural damage of the SI joints over time and will progress to definite AS. Another proportion of patients will remain in a stage of the disease without radiographic sacroiliitis, yet with inflammation on MRI.[12]

Spondyloarthritis features In the ASAS classification criteria, several SpA features are described. These features are called SpA features because they are frequently present in patients with SpA. Peripheral arthritis, enthesitis, especially heel enthesitis, and dactylitis are present in about 25% of SpA patients. Moreover, SpA is associated with extra-articular complaints such as anterior uveitis (23%), psoriasis (23%), and with IBD such as Crohn's disease and colitis ulcerosa (17%).[16] Additionally, elevated acute phase reactants (C-reactive protein and erythrocyte sedimentation rate) are observed in a number of patients with SpA, and sometimes an infection occurs preliminary to or simultaneously with the onset of complaints. Frequently, patient history shows that patients with SpA respond well to nonsteroidal anti-inflammatory drugs, unlike patients with mechanical back pain.[17] These clinical SpA features are inexpensive to obtain and can be used by all clinicians (**TABLE**).[6]

It is important to define a "positive" MRI. A definition of sacroiliitis as detected with MRI was developed based on a consensus among radiologists and rheumatologists in the ASAS/Outcome Measures in Rheumatology network MRI consensus group. An MRI is considered as "positive" if the areas of bone marrow edema (BME) are located at typical sites, i.e., they are periarticular to the SI joints. When only 1 BME lesion is visible on an MRI slice, it should be clearly visible on consecutive slices, otherwise it is not sufficient for a "positive" MRI. Enthesitis, capsulitis, or synovitis reflect active inflammation as well and are certainly compatible with SpA-related sacroiliitis, yet are not sufficient for a "positive" MRI if present without concomitant BME. Structural lesions such as sclerosis, erosions, periarticular

TABLE Definitions of spondyloarthritis features

Clinical criteria	Definition
IBP	IBP according to experts: 4 of 5 of the following parameters present: – age at onset <40 years – insidious onset – improvement with exercise – no improvement with rest – pain at night (with improvement upon getting up)
arthritis	past or present active synovitis diagnosed by a physician
family history	presence in first-degree or second-degree relatives of any of the following: – ankylosing spondylitis – psoriasis – uveitis – reactive arthritis – inflammatory bowel disease
psoriasis	past or present psoriasis diagnosed by a physician
IBD	past or present Crohn's disease or ulcerative colitis diagnosed by a physician
dactylitis	past or present dactylitis diagnosed by a physician
enthesitis	heel enthesitis: past or present spontaneous pain or tenderness at examination of the site of the insertion of the Achilles tendon or plantar fascia at the calcaneus
uveitis anterior	past or present uveitis anterior, confirmed by an ophthalmologist
good response to NSAIDs	24–48 hours after a full dose of an NSAID, the back pain is not present anymore or much better
lab- or imaging diagnostics	definition
HLA-B27	positive testing according to standard laboratory techniques
Verhoogde CRP	CRP above upper normal limit, after exclusion of other causes for elevated CRP concentration in the presence of back pain
sacroiliitis by X-rays	bilateral grade 2–4 or unilateral grade 3–4, according to the modified New York criteria
sacroiliitis by MRI	active inflammatory lesions of sacroiliac joints with definite bone marrow edema/ostiitis suggestive of sacroiliitis associated with spondyloarthritis

Abbreviations: IBD – inflammatory bowel disease, others – see FIGURE 3

fat depositions, and bony bridges are most likely to reflect previous inflammation and are visible on MRI, but are considered insufficient for the definition of sacroiliitis on MRI, particularly if they are small and seen only on MRI and not on X-rays.[18]

How to apply the new ASAS classification criteria?

The clinical SpA features are inexpensive and easy to collect. Because the ASAS axial SpA criteria consist of 2 arms, it is not necessary to collect all SpA features, which saves money and time, and is less invasive for patients. Generally, a radiograph to detect radiographic sacroiliitis is the first imaging step in all patients. If negative, either HLA-B27 status can be tested or an MRI can be performed, depending on how many clinical SpA features are present. In case of 2 or more clinical SpA features, one can choose to test HLA-B27 status; in case of 1 clinical SpA feature, one can choose to perform an MRI. In both cases, if HLA-B27 or MRI is positive, the patients fulfill the ASAS axial SpA criteria.

It is sufficient to perform an MRI only of the SI joints because this is where inflammation generally starts, and lesions rarely occur solely in the spine.[3] Furthermore, STIR images are equally capable of detecting BME as T_2 MRI after gadolinium administration. Only in cases of doubt and high suspicion, an additional scan after gadolinium can be considered. Abnormalities visible only on postcontrast images, such as enthesitis capsulitis and synovitis, are not sufficient for a positive MRI.[18]

According to the ASAS axial SpA criteria, a patient with chronic low back pain and age of less than 45 years at onset can be classified as having axial SpA if sacroiliitis on imaging (radiographs or MRI) plus at least 1 other SpA feature are present, or, in the absence of sacroiliitis on imaging, if HLA-B27 plus at least 2 other SpA features are present.[3] With a sensitivity of 82.9% and a specificity of 84.4% for the entire set of the ASAS criteria for axial SpA, these criteria perform better than the ESSG and Amor criteria, even after adding "sacroiliitis on MRI" to the latter.[2,3]

According to the ASAS peripheral SpA criteria, patients with peripheral arthritis (usually asymmetric arthritis and involving mainly the lower limb), enthesitis, or dactylitis can be classified as having peripheral SpA if at least 1 of the following features is present: uveitis, HLA-B27, preceding genitourinary or gastrointestinal infection, psoriasis, IBD, sacroiliitis on imaging (radiographs

or MRI), or at least 2 of the following features are present: arthritis, enthesitis, dactylitis, IBP, or a positive family history of SpA. In contrast to the axial SpA criteria, there is a distinction between SpA features that have a strong association with SpA and those that show a weaker association. The reason is that the entry criterion of arthritis, enthesitis, or dactylitis is less strong as the entry criterion (imaging or HLA-B27) in the axial SpA criteria.[9] These peripheral criteria with sensitivity of 77.8% and specificity of 82.8% are more promising than the expert opinion.[3,6]

Performance of ASAS axial spondyloarthritis criteria as diagnostic criteria The ASAS axial SpA criteria have been developed as classification criteria. However, if applied in a similar setting (rheumatology department with referral of patients suspected of SpA) they could also be used as diagnostic criteria. But in other settings, such as the general practitioner or a population study, more data need to be collected to assess whether they are sufficient to be used as diagnostic criteria.

Conclusion For the first time, 2 separate criteria sets for predominantly peripheral Spa and for predominantly axial SpA have been developed. The ASAS peripheral SpA criteria focus on patients with peripheral arthritis, enthesitis, and dactylitis, while the ASAS axial SpA criteria are intended to be applied in patients with predominantly complaints of the back, with or without peripheral complaints, with or without radiographic sacroiliitis. The ASAS criteria are useful as classification criteria in clinical trials; moreover, they are likely to be useful as diagnostic criteria, especially in patients with nonradiographic axial SpA at an outpatient rheumatolgy clinic. This may help prevent diagnostic delay and make an early diagnosis, which is very important for several reasons. First, an early diagnosis prevents unnecessary tests and inappropriate treatment.[19] Second, patients in an early stage of the disease, even those without definite radiologic sacroiliitis, can suffer as much pain and have as high disease activity as patients with established AS.[14] Finally, in an earlier stage of the disease, a specific treatment can be started, which, in turn, may improve work capability and everyday functioning of the patient.

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ARTYKUŁ POGLĄDOWY

Jak rozpoznawać spondyloartropatię według kryteriów klasyfikacyjnych ASAS 2010

Przewodnik dla lekarzy praktyków

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SŁOWA KLUCZOWE

kryteria klasyfikacyjne, rezonans magnetyczny, spondyloartropatia osiowa i obwodowa, zesztywniające zapalenie stawów kręgosłupa

STRESZCZENIE

Międzynarodowa grupa ASAS (ASsessment of SpondyloArthritis) opracowała niedawno kryteria klasyfikacyjne pacjentów ze spondyloartropatią (SpA) osiową z zapaleniem lub bez obecności radiologicznych cech zapalenia stawów krzyżowo-biodrowych w RTG oraz pacjentów ze SpA obwodową. Kryteria ASAS dla SpA osiowej składają się z 2 odrębnych części, można je stosować u osób z bólem krzyża (niemal codziennym trwającym >3 miesięcy). Podstawowe znaczenie w pierwszej części kryteriów mają badania obrazowe (RTG lub rezonans magnetyczny [*magnetic resonance* – MR]), a w drugiej – oznaczanie obecności antygenu HLA-B27. M umożliwia wykrycie czynnego zapalenia i zmian strukturalnych związanych ze SpA. Według kryteriów ASAS SpA osiową można rozpoznać u pacjentów z przewlekłym bólem krzyża, który rozpoczął się przed 45. rż., jeśli stwierdzi się zapalenie stawów krzyżowo-biodrowych w badaniu obrazowym (RTG lub MR) i ≥1 inną cechę SpA, lub też jeśli wykryje się antygen HLA-B27 i ≥2 inne cechy SpA.

Kryteria ASAS dla SpA obwodowej stosuje się u osób z zapaleniem stawów obwodowych (zwykle asymetrycznym, obejmującym głównie stawy kończyn dolnych), zapaleniem przyczepów ścięgnistych lub zapaleniem palców. Do spełnienia kryteriów klasyfikacyjnych SpA obwodowej niezbędne jest współistnienie ≥1 innej z poniższych cech SpA: zapalenia błony naczyniowej oka, HLA-B27, poprzedzającego zakażenia układu moczowo-płciowego lub przewodu pokarmowego, łuszczycy, choroby zapalnej jelit lub zapalenia stawów krzyżowo-biodrowych w badaniu obrazowym, lub ≥2 innych cech SpA: zapalenia stawów, zapalenia przyczepów ścięgnistych, zapalenia palców, zapalnego bólu krzyża lub SpA w wywiadzie rodzinnym.

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