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Juvenile Spondyloarthritis

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Abstract

Purpose of review—To provide a comprehensive update of the pathogenesis, diagnostic imaging, treatments, and disease activity measurements of juvenile spondyloarthritis (JSpA).

Recent findings—Genetic and microbiome studies have provided new information regarding possible pathogenesis of JSpA. Recent work suggests that children with JSpA have decreased thresholds for pain in comparison to healthy children. Additionally, pain on physical examination and abnormalities on ultrasound of the entheses are not well correlated. Treatment guidelines for juvenile arthritis, including JSpA, were published by the American College of Rheumatology and are based on active joint count and presence of sacroiliitis. Recent studies have established the efficacy of tumor necrosis factor inhibitors in the symptomatic treatment of axial disease, though their efficacy for halting progression of structural damage is less clear. Newly developed disease activity measures for JSpA include the Juvenile Arthritis Disease Activity Score and the JSpA Disease Activity index. In comparison to other categories of juvenile arthritis, children with JSpA are less likely to attain and sustain inactive disease.

Summary—Further microbiome and genetic research may help elucidate JSpA pathogenesis. More randomized therapeutic trials are needed and the advent of new composite disease activity measurement tools will hopefully allow for the design of these greatly needed trials.

Keywords

spondyloarthritis; ankylosing spondylitis; sacroiliitis; pediatric

Introduction

The spondyloarthropathies (SpA) are a heterogeneous group of disorders characterized by arthritis, enthesitis and increased risk of axial disease accompanied by overlapping genetic susceptibility. Juvenile SpA (JSpA) was last reviewed in this journal in 2006 (1). This article provides an update regarding classification criteria, pathogenesis, clinical manifestations, radiologic and disease activity assessments, treatment and prognosis of JSpA.

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Conflicts of interest: None

Classification

JSpA is a group of human leukocyte antigen (HLA) B27 associated disorders that begin at 16 years of age or younger. Both differentiated and undifferentiated forms are recognized. Seronegative enthesopathy and arthropathy syndrome is an undifferentiated form characterized by enthesitis with arthralgia or arthritis and the absence of rheumatoid factor and antinuclear antibodies. Differentiated forms of JSpA include enthesitis-related arthritis (ERA), juvenile psoriatic arthritis (JPsA), juvenile ankylosing spondylitis (JAS), reactive arthritis (ReA) and the arthropathies associated with inflammatory bowel disease (IBD). Three classification systems used for JSpA include 1) the International League of Associations for Rheumatology (ILAR) classification of juvenile idiopathic arthritis (JIA) (2), 2) the European SpA Study Group (ESSG) classification (3), and 3) the Amor criteria (4) (Table 1). Of these, the ILAR classification is used most often.

The ILAR classification of JIA (2) defines mutually exclusive categories of chronic arthritis. Most children with JSpA are classified in one of three categories: ERA, JPsA, or undifferentiated arthritis (features of both ERA and JPsA). Some of the conditions encompassed by JSpA not specifically included in this classification schema including ReA and IBD-related arthropathy. The ESSG criteria require inflammatory back pain or synovitis in addition to one of several other clinical criteria. The Amor criteria are based on a scoring system of laboratory, imaging, and clinical features.

In adults, SpA classification has shifted from distinguishing undifferentiated and differentiated disease toward criteria that identify patients with back pain who have “axial SpA” (AxSpA) versus those with peripheral manifestations only (5, 6). There are currently no criteria that make a similar distinction in children.

Genetics and Pathogenesis

Both genetic and environmental factors may contribute to the etiology of JSpA. HLA-B27 accounts for the majority (25%) (7) of known heritability in ankylosing spondylitis (AS), but the molecular mechanisms underlying this association remain unclear (8). HLA-B*27:05 is the most common subtype seen in JSpA (9). While HLA-B27 positivity is reported in more than 95% of adults with AS, recent JSpA studies demonstrate a lower prevalence of approximately 50% (10, 11). Several theories regarding the role of HLA-B27 in directly or indirectly stimulating an inflammatory response include: 1) HLA-B27 misfolding, 2) HLA-B27 binding of arthrogenic peptides, and 3) HLA-B27 dimerization (12). HLA-B27 misfolding triggers an unfolded protein response, which has been linked to increased production of IL-23, IFN β , and IL-1 in rats (12). IL-23 production stimulates expansion of Th17 cells that may be pathogenic in development of spondylitis (13). Furthermore, genes in the IL-23/IL-17 axis are thought to contribute to AS susceptibility.

Genome-wide association studies have also implicated the role of nonmajor histocompatibility complex (MHC) genes, including endoplasmic reticulum aminopeptidase 1 (ERAP1), in the development of AS via their interaction with HLA-B27 (7). The primary function of ERAP1 is peptide optimization for MHC class I binding and presentation. ERAP1 alleles that predispose to disease only do so in the presence of HLA-B27 (14).

Additionally, Lamot *et al* examined gene signatures in JSpA and found evidence to suggest that JSpA is a polygenic disease with involvement of TLR4, NLRP3, CXCR4 and PTPN12 (15).

Recently, the role of the microbiome in the pathogenesis of SpA has also been evaluated. Some hypothesize that HLA-B27 leads to mucosal immunodeficiency secondary to effects on intestinal permeability or alterations in the gut microbiome such as a loss of protective bacterial species (16). Using stool and blood samples Stoll *et al* demonstrated that in comparison to controls, ERA patients had decreased levels of *F. prausnitzii* (17). This bacteria has anti-inflammatory effects and decreased levels have been demonstrated in stool of patients with IBD (18). Additionally, another study demonstrated subclinical intestinal inflammation in three of five children with JSpA using magnetic resonance enterography (19).

Clinical Manifestations

Unlike other categories of juvenile arthritis, JSpA affects boys more than girls and peak age of onset is early adolescence. Defining characteristics of JSpA are enthesitis and axial arthritis. Enthesitis is inflammation at the attachment of tendons, ligaments, and joint capsule to bone that results in pain, swelling and tenderness. The most commonly tender entheses are the insertions of the patellar ligament at the inferior patella, plantar fascia at the calcaneus, and the Achilles tendon (10). Recent work suggests that children with JSpA have altered pain thresholds in comparison to healthy children and that tenderness at the entheses overestimates objective signs of inflammation visualized with imaging modalities such as ultrasound (20).

The arthritis is most commonly asymmetric, oligoarticular, involving the lower extremity large joints. Hip arthritis and tarsitis (midfoot inflammation) are highly suggestive of the diagnosis. Axial involvement has been reported in up to 30% of children within 15 months of diagnosis (21). As many as two-thirds of children develop axial disease within 10 years of diagnosis (22). Clinical features associated with sacroiliitis in children are higher active joint and entheses counts at diagnosis and hip arthritis (21, 23). In comparison to AS, inflammatory back pain is less common in children (24, 25) and has a low positive predictive value for the presence of sacroiliitis (26). In several studies sacroiliitis was identified in children without back pain (23, 26, 27).

The extra-articular manifestations of JSpA include acute anterior uveitis (AAU), bowel inflammation, psoriasis and cardiac disease. AAU is unilateral, acute inflammation with associated redness, pain and photophobia. Uveitis occurs in one-quarter of children with JSpA, similar to the incidence in adult-onset disease (28). Approximately two-thirds of adults with SpA have inflammatory bowel symptoms comparable to that seen in patients with IBD (29); similar prevalence rates have been reported in children (30). The exact prevalence of psoriasis in JSpA is unclear but psoriasis has been reported in 10–25% of SpA (31). Cardiac complications of SpA are well documented in adults but scarce in JSpA. According to Huppertz *et al* children with HLA-B27 associated arthritis are prone to endo-/

myocardial involvement including valvular inflammation (32). Stamato *et al* demonstrated aortic regurgitation in 8% of JSpA, similar to the incidence in adult-onset disease (33).

Imaging of the Entheses and Axial Joints

Low cost, accessibility, and non-invasiveness make ultrasound with Doppler (USD) an ideal method to evaluate arthritis and enthesitis in children with JIA, including JSpA. In a recent study of children with ERA, ultrasound-confirmed enthesitis, defined according to the Outcome Measures in Rheumatology Clinical Trial criteria was most common at the quadriceps tendon, common flexor tendon, and the Achilles tendon insertions (20) (Figure 1). In that study in comparison to USD, standardized examination of the entheses had poor accuracy and fair reliability. Children with ERA also had lower pain thresholds than normal healthy children at all entheses and control sites, even those without USD-confirmed inflammation. Another study that used USD to examine the entheses in children with all categories of JIA found that clinically silent enthesitis was detectable not only in children with ERA but also children with oligoarticular and polyarticular JIA (35). Further work needs to be done to determine the optimal ultrasound scoring method for enthesitis, the importance of clinically silent enthesitis, and the role of USD in monitoring disease activity.

Radiographs remain the gold standard for diagnosis of JAS. However, it is well established that radiographs are insensitive for the detection of early sacroiliitis. Bone marrow edema (BME) on magnetic resonance imaging (MRI) is visible prior to radiographic changes and is one of the accepted imaging modalities to classify AxSpA using the ASAS criteria (36). The presence of either subchondral or periarticular BME on short tau inversion recovery (STIR) imaging, or osteitis on T1 post-gadolinium images, are highly suggestive of active sacroiliitis. Importantly, the presence of enthesitis, synovitis, or capsulitis on MRI without concomitant BME is not considered sufficient evidence of active sacroiliitis (36).

The superiority of MRI over radiographs for establishing the diagnosis of JSpA in children presenting with symptoms suggestive of sacroiliitis was demonstrated in a recent study (37), though the evidence in favor of MRI was not as convincing as in adult studies (38). Although the use of gadolinium contrast was not specifically evaluated, the authors suggested gadolinium was not necessary for the evaluation of suspected sacroiliitis. In contrast, another retrospective study in children reported sacroiliac synovial enhancement without BME is frequent in children with JSpA (up to 30% of studies); the authors conclude that gadolinium should be used for optimal detection of sacroiliitis (39). Given the conflicting data regarding the evaluation of sacroiliitis in children, the current consensus (based upon adult studies) is to perform imaging that includes STIR sequences, but not gadolinium, given the risks associated with gadolinium administration (40).

Abnormalities of the spine are present in about 80% of adults with AS (41). Vendhan *et al* conducted a case-control study to identify lumbar spine abnormalities in children with ERA as compared to adolescents with inflammatory back pain. One or more abnormalities of the lumbar spine were found in 67% of the cases (42). Both apophyseal joint synovitis and interspinous ligament enhancement were more frequent in ERA cases compared to controls ($p=0.004$ and 0.04 respectively). Therefore spinal imaging should be considered in

symptomatic children to assess for inflammatory changes that may contribute to back pain in JSpA.

Treatments and Future Directions

The current treatment regimens for JSpA are based on those developed for adults with AS, rheumatoid arthritis and other categories of JIA. In the 2011 American College of Rheumatology Recommendations for the treatment of JIA, except those children with sacroiliitis, treatment algorithms for JSpA are grouped together with other JIA categories and are based upon the number of active joints (Table 2) (43).

Traditional disease-modifying anti-rheumatic drugs (DMARDs), including methotrexate and sulfasalazine, have established efficacy for peripheral arthritis in JIA. DMARDs have also been used in JSpA but have not been proven effective for axial disease or enthesopathy. TNF inhibitors have demonstrated efficacy for arthritis and enthesitis as well as symptomatic treatment of axial disease in JSpA (44–51). The efficacy of TNF inhibitors for halting progression of structural damage in children is less clear (45). Research in adults suggests that early inflammatory lesions in AS resolve following TNF inhibitor therapy and are not associated with the development of new syndesmophytes (52). It has also been reported that delays in starting TNF inhibitors are associated with increased odds of structural progression (53).

A number of small open label studies have been performed to evaluate the potential efficacy of B-cell-depleting therapy (rituximab) (54) and T-cell co-stimulation inhibition (abatacept) (55) in SpA. Interestingly, while rituximab was not effective in patients who had already received an anti-TNF agent, it was modestly effective in TNF-naïve patients (54). However, these studies did not provide evidence for the use of either non-TNF biologic agent as first-line therapy in adult SpA and have not been evaluated in JSpA. In contrast to rituximab and abatacept, for which there are only open-label data, the blockade of interleukin (IL)-6 was explored in two randomized, placebo-controlled trials in AS; neither of which was promising for the treatment of SpA (56).

There is growing evidence that the IL-12/23 and IL-17 axis is implicated in the pathogenesis of SpA. Drugs that target this axis include ustekinumab, an anti IL-12/23 human monoclonal antibody. It had a beneficial effect on axial disease in 20 adult AS patients (57). Secukinumab, an anti-IL-17A antibody, provided favorable results in a proof of concept trial in AS, including the open label extension phase up to 24 months (58, 59). In addition, apremilast, a PDE4 inhibitor, has been used in the treatment of psoriatic arthritis and there is research into its applicability to the treatment of SpA (60). Thus, there are multiple promising biologic agents on the horizon for the treatment of JSpA.

Physical and occupational therapy are also of benefit to many children with JSpA, particularly those with enthesitis and axial disease.

Disease activity measures

The Juvenile Arthritis Disease Activity Score (JADAS) is a composite score that consists of 4 elements: the physician assessment of disease activity, parent/patient global assessment of well-being, ESR, and active joint count (61). Children with ERA were included in the validation study of the JADAS but represented a minority (<1% of subjects). Cut-off values for defining remission, minimal disease and acceptable symptom state with the JADAS have been validated (62). The JSpA Disease Activity Score (JSpADA) is a continuous disease activity measure for children with JSpA that was retrospectively validated in a multicenter cohort of children (11). This index includes 8 items that are equally weighted and based primarily upon physician assessment (Table 3). It specifically includes measures of axial symptoms and enthesitis, which have been shown to independently predict poorer outcomes in this condition (63). The JSpADA needs to be validated in a prospective sample and cut-off values for defining remission and minimal disease activity should be determined.

Outcomes

The literature demonstrates an overall poorer prognosis for JSpA in comparison to other categories of JIA. Observational studies suggest that ongoing disease activity for greater than five years predicts disability and that disease remission occurs in less than 20% of children within five years of diagnosis (64, 65). In a study of 22 children with ERA who were treated with anti-TNF agents, none of the children were able to sustain remission off medication (50). Further, these children are less likely to achieve and to sustain inactive disease than other categories of JIA (50, 66). In comparison with the other categories of JIA, children with JSpA have more frequent and higher intensity pain and poorer health outcomes (63). Factors associated with an increased risk of continued disease activity include family history of AS, HLA-DRB1*08, ankle arthritis in the first 6 months of disease (67), HLA-B27 positivity, and hip arthritis (68).

Not only do JSpA patients have poorer outcomes compared to children with other forms of JIA but they also have worse outcomes than their adult counterparts. Chen *et al* compared clinical, functional, and radiographic outcomes at different ages of onset in patients with AS and found JAS was associated with worse functional outcome, global assessment scores, and poorer hip and sacroiliac radiographic scores (24). Other studies have shown a greater need for total hip arthroplasty among patients with juvenile-onset disease (69). Stone *et al* examined disability and functional impairment in adult versus pediatric AS. Patients with JAS reported more work related disability (24.7% vs. 20.9%) and more spinal deformity (17.2 % vs. 10.8%) compared to adult patients (70).

Conclusions

Our understanding of JSpA, including its pathogenesis and treatment, continues to evolve. The introduction of biologic therapies targeting TNF drastically changed the course of the disease and newer biologic agents targeting the IL-12/23 and IL-17 axis show future promise in the treatment of JSpA. This review highlights some of the advancements with regards to the diagnosis, imaging, treatment, and disease activity monitoring of JSpA. This

review also underscores the need for defining axial involvement and modified treatment guidelines to help improve the overall course of JSpA.

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Abbreviations

AAU	acute anterior uveitis
AS	ankylosing spondylitis
AxSpA	axial spondyloarthritis
BME	bone marrow edema
DMARD	disease-modifying anti-rheumatic drug
ERA	enthesitis-related arthritis
ERAP1	endoplasmic reticulum aminopeptidase 1
ESSG	European Spondyloarthropathy Study Group
HLA	human leukocyte antigen
IBD	inflammatory bowel disease
ILAR	International League of Associations for Rheumatology
JAS	juvenile ankylosing spondylitis
JADAS	Juvenile Arthritis Disease Activity Score
JIA	juvenile idiopathic arthritis
JPsa	juvenile psoriatic arthritis
JSpA	juvenile spondyloarthritis
JSpADA	JSpA Disease Activity Score
MRI	magnetic resonance imaging
NSAIDs	non-steroidal anti-inflammatory drugs
ReA	reactive arthritis
SEA	seronegative enthesopathy and arthropathy
SI	sacroiliac
SpA	spondyloarthropathy
STIR	short tau inversion recovery
TNF	tumor necrosis factor

USD

ultrasound with doppler

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Key Points

- HLA-B27, genes in the IL-23/IL-17 axis and the microbiome all likely contribute to the pathogenesis of JSpA.
- TNF blockers are first line treatment for children with sacroiliitis.
- New potential treatments include ustekinumab, secukinumab, and apremilast but additional clinical trials are warranted prior to their use in the pediatric population.
- Newly developed disease activity measures for JSpA include the JADAS and the JSpADA.
- In comparison to other categories of JIA, children with JSpA are less likely to attain and sustain inactive disease and they have higher pain intensity and poorer health outcomes.

Figure 1. Enthesitis in JSpA

Quadriceps tendon enthesitis in a 12-year-old boy. (A) Long, grayscale ultrasound image demonstrates focal hypoechoogenicity within the distal aspect of the quadriceps tendon (arrow) which is confirmed on the transverse image (B) with mild focal tendon enlargement (arrows). Long (C) and transverse (D) Power Doppler images demonstrates abnormal, increased signal within the tendon (dashed arrows) consistent with hyperemia. A small amount of joint fluid (arrow) is seen in D. *Original figures provided courtesy of Nancy Chauvin, MD, Philadelphia, PA.*

Table 1

Classification of JSpA

ILAR Categories of JSpA	ESSG Criteria for SpA	Amor Criteria
<p>Enthesitis Related Arthritis Arthritis and enthesitis <i>OR</i> Arthritis or enthesitis with at least 2 of the following:</p> <ul style="list-style-type: none"> Sacroiliac joint tenderness and/or inflammatory spinal pain Presence of HLA-B27 Onset of arthritis in a male over 6 years of age Family history in at least one firstdegree relative of ankylosing spondylitis, ERA, sacroiliitis with IBD, reactive arthritis or AAU Acute (symptomatic) anterior uveitis <p><i>Exclusions:</i></p> <ul style="list-style-type: none"> Psoriasis or a history of psoriasis in the patient or a first degree relative Presence of IgM RF on at least 2 occasions at least 3 months apart Systemic JIA in the patient 	<p>Inflammatory spinal pain or synovitis (asymmetric predominantly lower limb) and at least one of the following:</p> <ul style="list-style-type: none"> Psoriasis IBD (physician diagnosed and confirmed by endoscopy or radiography) Alternating buttock pain Urethritis, cervicitis, or diarrhea within one month before arthritis onset Enthesopathy at the Achilles tendon or plantar fascia Sacroiliitis (bilateral grade 2–4 or unilateral grade 3 or 4) Positive family history of AS, psoriasis, ReA, iritis, psoriasis, or IBD 	<p><i>SpA diagnosis if the sum of points is ≥ 6</i> Clinical Symptoms</p> <ul style="list-style-type: none"> Lumbar or dorsal pain at night or morning stiffness of lumbar or dorsal pain (1 point) Asymmetrical oligoarthritis (2 points) Buttock pain (1 point) Alternating Buttock pain (2 points) Sausage digit (2 points) Heel pain or other enthesopathy (2 points) Iritis (1 point) Nongonococcal urethritis or cervicitis within 1 month before arthritis onset (1 point) Acute diarrhea within 1 month before arthritis onset (1 point) Psoriasis, balanitis, or inflammatory bowel disease (2 points) <p>Radiologic Findings</p> <ul style="list-style-type: none"> Bilateral grade 2 or unilateral grade 3 sacroiliitis (3 points) <p>Genetic Background</p> <ul style="list-style-type: none"> Presence of HLA-B27 and/or family history of AS, ReA, uveitis, psoriasis, IBD (2 points) <p>Response to treatment</p> <ul style="list-style-type: none"> Improvement within 48 hours after NSAIDs or rapid relapse of pain after NSAID discontinuation (2 points)
<p>Psoriatic Arthritis Arthritis and psoriasis <i>OR</i> Arthritis plus at least 2 of the following:</p> <ul style="list-style-type: none"> Nail pitting or onycholysis Dactylitis Psoriasis in a first-degree relative <p><i>Exclusions:</i></p> <ul style="list-style-type: none"> Arthritis in an HLA-B27-positive male starting after age 6 years Personal or family history of AS, ERA, sacroiliitis with IBD, reactive arthritis, or acute anterior uveitis Presence of IgM RF on at least 2 occasions at least 3 months apart 		
<p>Undifferentiated Arthritis</p> <ul style="list-style-type: none"> Arthritis that fulfills none of the ILAR categories, or fulfills criteria in ≥ 2 categories 		

Inclusion and exclusion criteria for ILAR categories of SpA (2), ESSG SpA criteria (3) and the Amor criteria (4).
Adapted from [2], [3] and [4]

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Table 2

2011 ACR Recommendations for the Treatment of JIA

Treatment Group	Recommendations
History of arthritis 4 joints	<ul style="list-style-type: none"> • NSAID monotherapy recommended for patients with low disease activity, without joint contracture, and without features of poor prognosis but if active arthritis lasts > 2 months, add an additional agent • Intraarticular (IA) glucocorticoid injections recommended for all patients with active arthritis • Methotrexate (MTX) recommended: <ul style="list-style-type: none"> ➤ As initial treatment for patients with high disease activity + features of poor prognosis ➤ After initial IA injection, if high disease activity + features of poor prognosis ➤ After repeat IA injection in patients with moderate disease activity + features of poor prognosis <i>OR</i> low disease activity + features of poor prognosis • Sulfasalazine (SSZ) after IA injection or trial of NSAIDs is recommended for ERA patients with moderate or high disease activity • TNF-α inhibitor recommended for patients who have received: <ul style="list-style-type: none"> ➤ IA injection and 3 months of methotrexate at maximum tolerable dose and have moderate or high disease activity + features of poor prognosis ➤ IA injections and 6 months of methotrexate at maximum tolerable dose +high disease activity without features of poor prognosis • TNF-α inhibitor also recommended for patients with ERA who have received IA injections and adequate trial of SSZ and have moderate or high disease activity
History of arthritis 5 joints	<ul style="list-style-type: none"> • NSAID monotherapy uncertain and not to be continued > 2 months for active arthritis • MTX recommended as initial treatment for patients with high disease activity and patients with moderate disease activity + features of poor prognosis • Leflunomide (LFM) as initial treatment for patients with high disease activity and features of poor prognosis • TNF-α inhibitor recommended for patients who received MTX or LFM for: <ul style="list-style-type: none"> ➤ 3 months +moderate or high disease activity <i>OR</i> ➤ 6 months + low disease activity
Active sacroiliac arthritis	<ul style="list-style-type: none"> • TNF-α inhibitor recommended for: <ul style="list-style-type: none"> ➤ Patients with active sacroiliac arthritis who have received an adequate trial of NSAIDs and have high disease activity and features of poor prognosis ➤ Patients who received MTX for: <ul style="list-style-type: none"> - 3 months + high disease activity, <i>OR</i> moderate disease activity + features of poor prognosis - 6 months +moderate disease activity ➤ Patients who received SSZ for: <ul style="list-style-type: none"> - 3 months + moderate/high disease activity - 6 months +low disease activity with features of poor prognosis

Adapted from Beukelman *et al.* 2011 American College of Rheumatology recommendations for the treatment of juvenile idiopathic arthritis (43).

Table 3

JSpA Disease Activity Indices

JADAS -27		JSpADA Index	
Item	Scoring	Item	Scoring
Physician Global Assessment of Disease Activity <ul style="list-style-type: none"> 10-cm visual analog scale (VAS) where 0 is no activity and 10 is maximum activity 	0–10	Active joint count , includes any involved joint to a maximum of 10	0 joints = 0 1–2 joints = 0.5 >2 joints = 1
Parent/Patient Global Assessment of Well-Being <ul style="list-style-type: none"> 10-cm VAS where 0 is very well and 10 is very poor 	0–10	Active enthesitis count (includes any tender entheses to a max of 10; no weighing of particular entheses), mean $\pm$ SD	0 entheses = 0 1–2 entheses = 0.5 >2 entheses = 1
Count of Joints with Active Disease	0–27*	Pain , patient-reported over the past week, recorded on a VAS 0–10	0 = 0 1–4 = 0.5 5–10 = 1
		ESR or CRP level related to juvenile SpA activity	Normal = 0 1–2 times normal = 0.5 >2 times normal = 1
Normalized Erythrocyte Sedimentation Rate (ESR) <ul style="list-style-type: none"> Value normalized on 0–10 scale according to the formula: $[\text{ESR (mm/hr)} - 20]/10$ Before making the calculation, ESR values <20 mm/hr are converted to 0 and ESR values >120 mm/hr are converted to 120 	0–10	Morning stiffness , >15 minutes	Absent = 0 Present = 1
		Clinical sacroiliitis , defined as the presence of 2 of the following: tenderness on examination, positive Patrick's test or FABER test, and inflammatory back pain	Absent = 0 Present = 1
		Uveitis	Absent = 0 Present = 1
		Back mobility , abnormal back mobility defined as modified Schober test <20 cm	Normal = 0 Abnormal = 1
Score range	0–57	Score range	0–8

Elements and scoring for the Juvenile Arthritis Disease Activity Score (JADAS) and the JSpA Disease Activity Score (JSpADA). ESR: erythrocyte sedimentation rate; CRP: C-reactive protein; FABER: flexion abduction external rotation.

* JADAS 10, 27, and 71 have active joint counts of 0–10, 0–27, and 0–71, respectively.