Axial and Peripheral SpA: A Rheumatic Duet

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Information

• This scientific session is sponsored by Novartis Medical Affairs; and
• For any questions, please see Novartis associates here in the room or at Booth 26
Learning Objectives

1. Recognize that spondyloarthritis (SpA) is a spectrum of disease consisting of axial and peripheral subtypes.

2. Differentiate SpA from other rheumatic diseases by highlighting enthesitis, bone erosion, and osteoproliferation.

3. Identify the features of axial and peripheral SpA in patients to aid earlier diagnosis.

4. Explore sex differences in axial spondyloarthritis (axSpA) disease presentation.
Disclosures for Grace Wright, MD, PhD

- Speaker bureau, advisory boards, or consultant for AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Crescendo Bioscience, Genentech, Horizon Pharma, Janssen Biotech, Lilly, Mallinckrodt Pharmaceuticals, Medac Pharma, Novartis, Pfizer, Sanofi Genzyme Regeneron, UCB
The spondyloarthritis (SpA) spectrum is comprised of axial and peripheral subtypes

Spondyloarthritis (SpA) is a group of diseases with many subtypes

AS = ankylosing spondylitis; AxSpA = axial spondyloarthritis; IBD-SpA = inflammatory bowel disease and spondyloarthritis; SpA = spondyloarthritis; AS = ankylosing spondylitis; IBD = inflammatory bowel disease; PsA = psoriatic arthritis; nr-AxSpA = non-radiographic axial spondyloarthritis; PsA = psoriatic arthritis; ReA = reactive arthritis; SpA = spondyloarthritis.

Is SpA a spectrum of diseases or one heterogenous disease?

“Seronegative spondyloarthropathies: to lump or split?”

P Nash, P J Mease, J Braun, D van der Heijde

“Moll et al initially included Whipple’s disease in their classification—a disease, which when studied as its own entity rather than “lumped” in a group, has had its aetiological agent defined allowing appropriate therapy and cure. We would like to agree…”¹


Is SpA a spectrum of diseases or one heterogenous disease?

REVIEW

“Are Spondylarthritides Related but Distinct Conditions or a Single Disease With a Heterogenous Phenotype?”

“The available evidence suggests a common pathophysiologic foundation for SpA as a whole and thereby supports the concept that SpA is a single disease with a heterogeneous phenotype. However, this conclusion is tempered by the facts that our understanding of the cellular and molecular pathways driving SpA pathogenesis are still very incomplete…”1

D Baeten, M Breban, R Lories, G Schett, J Sieper

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REVIEW

"Are Spondylarthritides Related but Distinct Conditions or a Single Disease With a Heterogenous Phenotype?"

D Baeten, M Breban, R Lories, G Schett, and J Sieper

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SpA = spondyloarthritis

The pathophysiology of articular manifestations is largely similar across subtypes, but what determines the exact phenotype in an individual patient remains unknown.¹

Emerging data suggest that axial and peripheral disease may be driven by slightly different mechanisms.¹

## How common is SpA?

### National Arthritis Data Workgroup (2005 US Census data)

<table>
<thead>
<tr>
<th>Disease</th>
<th>Prevalence in US adults</th>
</tr>
</thead>
<tbody>
<tr>
<td>RA</td>
<td>1.3 million (0.6%)</td>
</tr>
<tr>
<td>SpA</td>
<td>0.6 million to 2.4 million (0.3 to 1.3%)</td>
</tr>
</tbody>
</table>

### Subtype (criteria) | Prevalence in US adults

<table>
<thead>
<tr>
<th>SpA, 2009-2010 (Amor)</th>
<th>0.9%</th>
</tr>
</thead>
<tbody>
<tr>
<td>SpA, 2009-2010 (ESSG)</td>
<td>1.4%</td>
</tr>
<tr>
<td>axSpA, 2010 (ASAS)</td>
<td>0.7%</td>
</tr>
<tr>
<td>PsA (various)</td>
<td>0.06 to 0.25%</td>
</tr>
</tbody>
</table>

The prevalence of SpA is comparable or higher than that of RA, yet it remains less known.\(^2,5\)

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AxSpA = axial spondyloarthritis; SpA = spondyloarthritis; AS = ankylosing spondylitis; PsA = psoriatic arthritis; RA = rheumatoid arthritis; US = United States.
How does SpA affect patients?

SpA occurs in young adults at the peak of their productive lifespan\(^1\)

Associated with burden in:\(^1\)

- 49% report disability\(^1,a\)
- 36% experienced limitations hindering development/career\(^1,a\)
- 21% changed, left, or lost their job due to SpA\(^1,a\)

SpA = spondyloarthritis.

a. Data from the 2013 ATLANTIS survey of 770 respondents from 17 regions in Italy. b. Other reasons included vacation or family commitments.

What are the distinguishing features of SpA?

- **Enthesitis**
- **PsO**
- **Bone Formation**
- **Axial disease**
- **Uveitis**
- **Peripheral arthritis**
- **Dactylitis**


Enthesitis is an important early feature in SpA

One of the first signs of musculoskeletal involvement in patients with psoriasis (before joint involvement) is enthesophyte formation in the peripheral joints (indicated by red arrows), indicating that enthesitis may be an important early feature in psoriatic disease.¹,²

SpA = spondyloarthritis.


Permission granted by Simon D, et al.¹
Mechanical stress is a key trigger for enthesitis

Enthesitis is triggered by a complex interplay between mechanical stress, microbiome, and genetic predisposition.¹-³

- **Mechanical stress**
- **Genetics** (e.g., HLA-B27)
- **Impaired barrier function** (e.g., microbial stress)

HLA-B27 = Human leukocyte antigen B27.

Anatomic differences between spinal and peripheral entheses

There may be anatomical and immunological differences between axial and peripheral enthesitis and downstream disease manifestations\(^1\)

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Inflammation in axial and peripheral entheses

**Axial enthesitis**

- New bone formation
- Vertebra
- Intervertebral disc
- Ligament
- Translocation of PAMPs from gut and skin

**Peripheral enthesitis**

- Biomechanical stress or trauma
- IL-17
- IL-23
- IL-22
- TNF-α

- Pathologic bone formation
- Osteoprogenitor
- IL-17, TNFα, RANKL
- Osteoblasts

Bone remodeling is tightly linked to enthesitis

- Structural changes in SpA are unique and severe
- Skeletal damage is a consequence of bone destruction and aberrant bone formation originating from the entheses and can lead to total ankylosis or “bamboo spine”

Bone formation

Bone erosion

Bone remodeling is tightly linked to enthesitis

Enthesal inflammation is closely linked to osteitis and new bone formation

- Extensive transcortical microvessels (TCVs) enable communication between the bone marrow and the enthesis\(^1\)

- TCVs become widened following stress/injury, leading to efflux of immune cells from the bone marrow into the enthesis\(^1\)

MSC = mesenchymal stem cell; PsA = psoriatic arthritis; TCV = transcortical microvessels.

Enthesal inflammation is closely linked to osteitis and new bone formation

MSC = mesenchymal stem cell; PsA = psoriatic arthritis; TCV = transcortical microvessels.

Enthesal inflammation is closely linked to osteitis and new bone formation

MSC = mesenchymal stem cell; PsA = psoriatic arthritis; TCV = transcortical microvessels.


Abnormal vascularization at the cortical junction of a SpA patient with plantar fascia enthesitis

Systemic bone erosion in SpA

• Increased bone resorption and decreased bone formation leads to bone loss\(^1\)

• Premature systemic bone loss; trabecular and cortical bone are lost, resulting in osteopenia and/or osteoporosis\(^2\)
IL-17 and IL-23 initiate entheseseal inflammation and new bone formation

- Bone formation tends to be localized at entheseseal sites\(^1\)
- Resembles a response-to-injury process; a cartilage scaffold is formed and remodeled into bone\(^1\)

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IL = interleukin; MSC = mesenchymal stem cell.
Proinflammatory immune cells produce cytokines that contribute to clinical manifestations of SpA1-5

Proinflammatory immune cells produce cytokines that contribute to clinical manifestations of SpA1-5

SpA = spondyloarthritis; CD = cluster of differentiation; IFNγ = interferon gamma; IL = interleukin; TGF-β = transforming growth factor β; Th cell = T helper cell; TNFα = tumor necrosis factor-α.

Discussion

1. How often do you see enthesitis in your practice?

2. Is enthesitis the first inflammatory lesion you observe in SpA?
Axial and Peripheral Manifestations of PsA
Undiagnosed PsA is prevalent among patients with PsO

PREPARE Study (Prevalence of PsA in Adults With PsO: An Estimate From Dermatology Practice)¹

Patients with PsO in dermatologists’ offices (N=949)

Rheumatologists examined patients using:
• Medical history
• Physical examination
• Laboratory test findings

30% of patients (n=285) received a clinical diagnosis of PsA

41% (n=117) of patients had not previously been diagnosed with PsA

Patients with PsO also showed a higher prevalence of enthesopathy, which may be an early sign of PsA²

Dermatologists can play an important role in screening patients with PsO for early signs of PsA and actively monitoring for signs of joint or arthritic involvement³

PsA = psoriatic arthritis; PsO = psoriasis.
PREPARE, Prevalence of Psoriatic Arthritis in Adults With Psoriasis: An Estimate From Dermatology Practice.
Various clinical manifestations of PsA

Patients with PsA face a multifaceted disease involving multiple clinical domains

<table>
<thead>
<tr>
<th>Peripheral arthritis²</th>
<th>Enthesitis³</th>
<th>Dactylitis⁴</th>
<th>Skin⁵,⁶</th>
<th>Nails⁷</th>
<th>Axial disease⁸</th>
</tr>
</thead>
<tbody>
<tr>
<td>Permission granted by ACR.²</td>
<td>Permission granted by ACR.³</td>
<td>Permission granted by ASAS.⁴</td>
<td>Permissions granted by Wozel G et al. and Menter A, et al⁵</td>
<td>Permission granted by Manhart R et al.⁷</td>
<td>Permission granted by Ritchlin CT et al.⁸</td>
</tr>
</tbody>
</table>

96%⁸ 30% to 50%⁸ 40% to 50%⁸ 100%⁸ >80%⁸ 25 to 70%⁹

PsA = psoriatic arthritis.

Peripheral arthritis in PsA

Presentation

- Involves the peripheral joints: elbows, wrists, hands, and feet\(^1,2\)
- Leads to joint erosion, joint space narrowing, bony proliferation, osteolysis, and synovitis\(^3\)
- Ranges from none through to monoarthritis, to oligoarthritis (≤4 joints), to polyarticular (>4 joints) destructive erosive arthritis\(^1,2\)

Patient impact

- Pain and irreversible deformities can result in loss of function\(^2\)
- Damage is progressive in majority of patients\(^4\)
  - Median of 0.42 peripheral joints/year (range: 0-7.2)\(^4\)

**Enthesitis**

**Presentation**
- Characterized by pain and swelling at the site of tendon and ligament insertion into the bone\(^1\)\(^-\)\(^3\)
- Common sites: Achilles tendon, plantar fascia, and greater trochanter\(^4\)
- Reported to occur in 35% to 50% of patients with PsA\(^5\)

**Patient impact**
- PsA patients with enthesis face a greater burden than those without enthesis, reporting greater pain, fatigue, and impairment of work and activity\(^6\)

PsA = psoriatic arthritis.

Dactylitis

Presentation
• Diffuse swelling of the entire finger or toe (sausage digit)\textsuperscript{1,2}
  • Swelling can be acute (inflammation/pain) or chronic (without inflammation)\textsuperscript{3}
• Associated with erosive joint damage\textsuperscript{3}
• 32\%-48\% of patients with PsA have dactylitis\textsuperscript{5}
  • 50\% of patients have multiple digits involved simultaneously\textsuperscript{5}

Patient impact
• Fatigue, pain, and swelling impairs work and non-work activities\textsuperscript{4}
• Morbidity related to dactylitis increases with time\textsuperscript{5}

PsA = psoriatic arthritis.

Skin

Presentation

• Papules, patches, and plaques, sharply marginated with silvery buildup of dead skin cells (scales)\textsuperscript{1}

• Common sites: scalp, nails, trunk, elbows, and knees\textsuperscript{2}

• All patients with PsA have PsO\textsuperscript{2}
  • ~10%-37% of PsO patients develop PsA, which may precede skin disease in some cases\textsuperscript{3}

Patient impact

• Even moderate amounts of psoriatic skin involvement are associated with a greater disease burden of PsA, with greater reported pain, fatigue, and higher HAQ scores\textsuperscript{3}

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HAQ = Health Assessment Questionnaire; PsA = psoriatic arthritis; PsO = psoriasis.

Nail

Presentation

- Pitting, discoloration, crumbling, nail bed separation, changes in nail shape/thickness, horizontal lines
  1
- Affects ~ 80% of PsA patients due to close association between DIP joints and nail matrix

Patient impact

- Associated with discomfort and pain
- Can lead to functional impairment and psychological stress

DIP = distal interphalangeal; PsA = psoriatic arthritis.

Axial disease

Presentation

- Inflammation in the axial skeleton
- Back pain, stiffness, restriction in spinal mobility, sacroiliitis, spondylitis, and syndesmophyte formation
- Prevalence of axial PsA ranges from 25% to 75% of patients with PsA; may be asymptomatic

Patient impact

- PsA patients with axial involvement had a higher likelihood of higher disease activity and worse quality of life compared to those with mainly peripheral involvement in PsA.
Axial involvement in PsA is prevalent

- 2-5% of patients with PsA have solely axial disease\(^1\)
- 15% of patients with PsA who did not have axial involvement at presentation developed axial PsA during 10 years of follow-up\(^2\)
- Increased risk of developing axial disease at an early stage:\(^1\)
  - 40-50% of patients with PsA are HLA-B27 positive\(^3\)
  - Presence of radiographic damage to peripheral joints
  - Increased ESR

PsA = psoriatic arthritis; ESR = erythrocyte sedimentation rate; HLA-B27 = human leukocyte antigen B27.

PsA is a multifaceted disease involving multiple clinical domains

- **Peripheral arthritis**
- **Enthesitis**
- **Dactylitis**
- **Skin**
- **Nails**
- **Axial disease**

PsA = psoriatic arthritis.

Discussion

1. How often are PsA patients with solely axial pain misdiagnosed with fibromyalgia?

2. How frequently are PsA patients with solely peripheral manifestations misdiagnosed with osteoarthritis?
Axial and Peripheral Manifestations of axSpA
Disclosures for Reeti Joshi, MD

• Reeti Joshi has received consulting and speaker fees from AbbVie, Celgene, Novartis, Sanofi Genzyme and UCB. She is also adjunct faculty at Baylor College of Medicine, Houston.

• This is a non-CME, unbranded, disease state presentation developed by Dr. Joshi and sponsored by Novartis Pharmaceuticals Corporation.
Subclinical process in genetically predisposed patients

Inflammatory back pain

nr-axSpA

Quiescent disease activity

Nonprogressing AS

The terms AS and nr-axSpA are distinguished by the degree of “radiographic sacroiliitis” assessed by conventional radiography.

These terms should only be used for classification of patients with axSpA and not as separate diagnoses.

Natural history of axSpA includes radiographic (AS) and nr-axSpA


axSpA = axial spondyloarthritis; nr-axSpA = nonradiographic axial spondyloarthritis; AS = ankylosing spondylitis.
Is axSpA underdiagnosed?

Axial spondyloarthritis (axSpA) = spondyloarthritis involving the axial skeleton; nonradiographic axial spondyloarthritis (nr-axSpA) = axSpA without radiographic evidence of sacroiliac joint or spine involvement.


Many patients with axSpA are misdiagnosed with RA.
Morning stiffness and joint involvement are common between the two.

### Morning Stiffness
- Reported in 90.4% of patients diagnosed with axSpA, with duration ≥30 minutes in 76% of patients

### ≥1 Swollen Joints
- Observed in 20.3% of patients with axSpA

axSpA = axial spondyloarthritis; nr-axSpA = nonradiographic axial spondyloarthritis; AS = ankylosing spondylitis; RA = rheumatoid arthritis.
Patients with axSpA experience a delay between symptom onset and diagnosis

- Delays in diagnosis of axSpA result in prolonged pain, stiffness, fatigue, decreased mobility, irreversible new bone formation, loss of spinal function, and reduced QoL.

In one study, 60% of patients developed syndesmophytes and ankylosis in the spine.

20 to 30% of patients develop structural changes.

Symptom onset 2 years 10 years

Delay in Diagnosis
(Years)

Symptom Duration

Disease Duration

MEN WOMEN

axSpA = axial spondyloarthritis; QoL = quality of life.

Features of axSpA

Chronic back pain (> 3 months)

Mechanical

Inflammatory

Presence of other SpA features

Psoriasis  Uveitis  Sacroiliitis and spondylitis  Peripheral joint involvement (oligo)arthritis  Enthesitis  Inflammatory bowel disease  Good response to NSAIDs  Positive family history

axSpA, axial spondyloarthritis; NSAIDs, nonsteroidal anti-inflammatory drugs; SpA, spondyloarthritis.

axSpA patients can present symptoms across different axial sites

- The most typical symptom of axSpA is IBP\(^1\)
- Thoracic spine, cervical spine, and chest can also be affected\(^1\)

Female patients present IBP at a lower frequency\(^2\)
73 vs 89% (F vs. M)

<table>
<thead>
<tr>
<th>Pain Locations</th>
<th>Men</th>
<th>Women</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>25%</td>
<td>45.2%</td>
</tr>
<tr>
<td></td>
<td>69.4%</td>
<td>83.9%</td>
</tr>
<tr>
<td></td>
<td>26.9%</td>
<td>43.5%</td>
</tr>
</tbody>
</table>

Axial pain in thoracic, lumbar, and SIJ tends to be more common in women\(^3\)

F = female; IBP = Inflammatory back pain; Lx = lumbar; M = male; SIJ = sacroiliac joint; Tx = thoracic.

\(^*\) Denotes significant difference between the sexes

axSpA patients can present symptoms across the body including peripheral sites

- Peripheral manifestations—arthritis and enthesitis—can occur at any time in the course of the disease\(^1\)
  - Predominantly lower limbs, asymmetrically
  - Dactylitis is less frequent but may also occur

<table>
<thead>
<tr>
<th>SpA diagnosis by ASAS criteria(^2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>51% of patients diagnosed using axial criteria also met the peripheral criteria</td>
</tr>
</tbody>
</table>

- Axial Cohort (73.2%)
- Peripheral Cohort (26.8%)

- 64% had history/presence of peripheral arthritis
- 62% had history/presence of enthesitis
- 8% had history/presence of dactylitis

Enthesitis is more common and severe in females\(^3,4\)
67.9% vs 41.1% (F vs. M)

axSpA = axial spondyloarthritis; SpA = spondyloarthritis; ASAS = assessment of spondyloarthritis international society; F = female; M = male.

axSpA tends to affect the lower extremities

- In a whole-body MRI study of axSpA, inflammatory lesions were most often present in the lower thoracic, lumbar spine, and lower extremities\(^1\)
- Enthesitis primarily affects the lower limbs, which are exposed to higher mechanical forces than the upper limbs\(^1,2\)

\(axSpA = \text{axial spondyloarthritis}; \text{MRI} = \text{magnetic resonance imaging.}\)

**axSpA patients can present symptoms across the body including peripheral sites**

- Extra-articular involvement includes:¹
  - **Uveitis**
    - Typically acute anterior, limited in duration, unilateral, and frequently alternating between eyes
  - **Psoriasis**
  - **IBD**

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Genetic susceptibility in PsA and AS

• Axial disease in PsA is more commonly associated with other HLA genes than with HLA-B27¹

• HLA-B27 positivity
  • 83-90% of patients with AS²,³
  • 74-86% of patients with nr-axSpA⁴-⁶
  • Disease occurs 5 years earlier in HLA-B27(+) patients than in those who are HLA-B27(-)⁷

HLA-B27 is commonly associated with PsA and AS¹

Psoriatic arthritis
  • HLA-C*06:02
  • HLA-C*12−HLA-B*38 haplotype
  • HLA-C*06−HLA-B*57 haplotype
  • KIR2DS2
  • TRAF2IP2
  • TNI1P
  • REL
  • IFIH1
  • NFKBIA
  • IL-13 genes
  • IFNLR1
  • HLA-B*39
  • HLA-B*08
  • HLA-B*38
  • HLA-Cw*07:02

Ankylosing spondylitis
  • HLA-B*13:02
  • HLA-B*40:01
  • HLA-B*40:02
  • HLA-B*47:01
  • HLA-B*51:01
  • ERAP1
  • ERAP2
  • NPEPPS
  • IL-23−IL-17 pathway genes

HLA-B27 positivity is more common in male axSpA patients⁸
  • 80% vs. 60% (M vs. F)

AS = ankylosing spondylitis; F = female; HLA = human leukocyte antigen; HLA-B27 = human leukocyte antigen B27, M = male; nr-axSpA = nonradiographic axial spondyloarthritis; PsA = psoriatic arthritis.

Imaging of the SI joint is critical for accurate and early diagnosis of axSpA

- Radiography of the SI joints is recommended as the first imaging method to diagnose sacroiliitis\(^1\)
- Limitations:\(^1\)
  - Structural changes may take months to years to occur
  - Interpretation is challenging
- MRI of the SI joint is required for normal or ambiguous radiographic results in the context of a possible diagnosis of axSpA\(^1\)
- Early non-radiographic stage may demonstrate normal radiography\(^2\)
- MRI can detect acute inflammatory changes (bone marrow edema) in the absence of radiographic sacroiliitis\(^2\)

axSpA = axial spondyloarthritis; SI = sacroiliac; MRI = magnetic resonance imaging.

The subgroups of axSpA - nr-axSpA and AS - are differentiated by the presence of structural change in the sacroiliac spine\(^1\). Out of a cohort of patients who met ASAS criteria for axSpA, ratio of patients with AS to those with nr-axSpA is 1:1\(^2\).

Females have slower progression of radiographic damage\(^3,4\).
- Less thoracic and lumbar spine radiographic severity
- Lower BASRI scores

**Radiographic distinction between nr-axSpA and AS**

- Axial spondyloarthritis (ASAS criteria)
- Nonradiographic stage
- Radiographic stage
- X-ray negative sacroiliitis
- X-ray positive sacroiliitis
- X-ray positive sacroiliitis and spinal changes

Adapted with permission from Sieper J, et al.\(^1\)

axSpA = axial spondyloarthritis; nr-axSpA = nonradiographic axial spondyloarthritis; AS = ankylosing spondylitis; ASAS = assessment of spondyloarthritis international society; BASRI = bath ankylosing spondylitis radiology index.

Radiographic changes in PsA and axSpA

- Symmetric lesions are characteristic for axSpA, while unilateral, asymmetric sacroiliitis point to other forms of SpA – most commonly psoriatic arthritis\(^2,4\)
- Asymmetric distribution of syndesmophytes is more common in cases of PsA\(^3\)
- Severity of radiographic axial disease may be greater in AS than PsA\(^5\)

PsA = psoriatic arthritis; axSpA = axial spondyloarthritis.

Women have a unique presentation and burden of disease

- More diagnosis delay\(^1\)
- Poorer quality of life\(^8\)
- Less likely to have children than women in the general population\(^2\)
- Misdiagnoses of fibromyalgia and psychosomatic disorder\(^7\)
- More pronounced enthesitis, disease severity, and peripheral symptoms\(^3\)-\(^6\)
- Lower inflammatory markers despite comparable or higher disease severity score\(^6\)

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axSpA has a significant patient burden

- Patients with axSpA have **poorer QoL** than the general population\(^1\)
- Patients with axSpA are more likely to be **unmarried or divorced**\(^1\)
- Patients with axSpA are more than twice as likely to be **too disabled to work** as the general population\(^1\)
- Scores of disease status correlate with **anxiety, depression, and health status**\(^1\)
- High costs due to **functional disability** and **disease management**\(^2\)

axSpA = axial spondyloarthritis; QoL = quality of life.

nr-axSpA patients share a comparable degree of disease burden with AS patients

nr-axSpA

- Enthesitis
- Presenteeism and activity impairment

Experience worse:
- Pain and fatigue
- Disease activity and function
- Quality of life

AS

- Longer disease duration
- Worse structural damage
- Worse spinal mobility

nr-axSpA = nonradiographic axial spondyloarthritis; AS = ankylosing spondylitis.
Peripheral disease manifestations contribute significantly to disease activity

<table>
<thead>
<tr>
<th></th>
<th>Purely axial disease</th>
<th>Peripheral and axial disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient’s global assessment</td>
<td>52</td>
<td>61</td>
</tr>
<tr>
<td>Physician’s global assessment</td>
<td>44</td>
<td>53</td>
</tr>
<tr>
<td>Disease activity (BASDAI)</td>
<td>4.4</td>
<td>5.4</td>
</tr>
<tr>
<td>Disease activity (ASDAS-CRP)</td>
<td>2.6</td>
<td>3.0</td>
</tr>
</tbody>
</table>

BASDAI = bath ankylosing spondylitis disease activity index; ASDAS = ankylosing spondylitis disease activity score; CRP = C-reactive protein.

Discussion

1. How do female axSpA patients present differently compared to men?

2. What imaging modalities do you use in your axSpA patients to help in diagnosis, prognosis, and disease management?

3. How often are axSpA patients with peripheral disease presentation misdiagnosed?
**Peripheral and axial spondyloarthritis share many similar features**

<table>
<thead>
<tr>
<th>Pathophysiology</th>
<th>Peripheral</th>
<th>Axial</th>
</tr>
</thead>
<tbody>
<tr>
<td>IL-17</td>
<td>Important&lt;sup&gt;6,7&lt;/sup&gt;</td>
<td>Important&lt;sup&gt;6&lt;/sup&gt;</td>
</tr>
<tr>
<td>IL-23</td>
<td>Involved&lt;sup&gt;6&lt;/sup&gt;</td>
<td>Less involved&lt;sup&gt;6&lt;/sup&gt;</td>
</tr>
<tr>
<td>TNF</td>
<td>Important&lt;sup&gt;6,7&lt;/sup&gt;</td>
<td>Important&lt;sup&gt;6&lt;/sup&gt;</td>
</tr>
<tr>
<td>HLA-B27 positivity</td>
<td>Sometimes present</td>
<td>Common</td>
</tr>
<tr>
<td></td>
<td>• 40-50% of patients with PsA&lt;sup&gt;1&lt;/sup&gt;</td>
<td>• 83-90% AS patients&lt;sup&gt;1,2&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• 74-86% nr-axSpA patients&lt;sup&gt;3-5&lt;/sup&gt;</td>
</tr>
<tr>
<td>Bone changes</td>
<td>Present&lt;sup&gt;9&lt;/sup&gt;</td>
<td>Present&lt;sup&gt;8&lt;/sup&gt;</td>
</tr>
<tr>
<td>Bone marrow edema</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bone erosion</td>
<td>Hallmark&lt;sup&gt;8,9&lt;/sup&gt;</td>
<td>Hallmark&lt;sup&gt;8&lt;/sup&gt;</td>
</tr>
<tr>
<td>Bone formation</td>
<td>Hallmark&lt;sup&gt;9&lt;/sup&gt;</td>
<td>Hallmark&lt;sup&gt;8&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

IL = interleukin; TNF = tumor necrosis factor; HLA = human leukocyte antigen; AS = ankylosing spondylitis; nr-axSpA = nonradiographic axial spondyloarthritis; PsA = psoriatic arthritis.

Peripheral and axial spondyloarthritis share many similar features

<table>
<thead>
<tr>
<th></th>
<th>Peripheral</th>
<th>Axial</th>
</tr>
</thead>
<tbody>
<tr>
<td>**Axial</td>
<td>Sacroiliitis</td>
<td>Common(^1)</td>
</tr>
<tr>
<td>manifestations</td>
<td>Spondylitis</td>
<td>Common(^{1,4})</td>
</tr>
<tr>
<td>**Peripheral</td>
<td>Peripheral arthritis</td>
<td>Hallmark(^1)</td>
</tr>
<tr>
<td>manifestations</td>
<td>Enthesitis</td>
<td>Common(^{1,4})</td>
</tr>
<tr>
<td></td>
<td>Dactylitis</td>
<td>Common(^{1,4})</td>
</tr>
<tr>
<td><strong>Extra-articular manifestations</strong></td>
<td>Psoriasis</td>
<td>Hallmark(^1)</td>
</tr>
<tr>
<td></td>
<td>Uveitis</td>
<td>Sometimes present(^1)</td>
</tr>
<tr>
<td></td>
<td>IBD</td>
<td>Sometimes present(^1)</td>
</tr>
</tbody>
</table>

### Key differences in axial and peripheral SpA

<table>
<thead>
<tr>
<th></th>
<th>Peripheral SpA</th>
<th>Axial SpA</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age of onset</strong></td>
<td>Mid to late 30s</td>
<td>Early 20s</td>
</tr>
<tr>
<td><strong>Severity and pain</strong></td>
<td>Less</td>
<td>More</td>
</tr>
<tr>
<td><strong>Sacroiliitis</strong></td>
<td>Less symmetrical</td>
<td>More symmetrical</td>
</tr>
<tr>
<td><strong>Syndesmophytes</strong></td>
<td>Less symmetrical</td>
<td>More symmetrical</td>
</tr>
</tbody>
</table>

SpA = spondyloarthritis.

<table>
<thead>
<tr>
<th>Conclusion</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>SpA is a spectrum of disease that contains both axial and peripheral symptoms</strong></td>
<td></td>
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<tr>
<td><strong>Enthesitis and new bone formation are unique features of SpA</strong></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td><strong>Axial and peripheral SpA share many common features as well as some key differences</strong></td>
<td></td>
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<tr>
<td><strong>Sex distinctions of axSpA are present across facets of the disease</strong></td>
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</tr>
</tbody>
</table>
Thank you for attending!
Let us know what you thought of this symposium
education.novartis.com/survey

Any questions?
Visit the Novartis Medical Affairs Booth 26
for additional questions