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Improving the Diagnosis and Treatment of Axial Spondyloarthritis Across a Wider Patient Population

Adopting a patient-centric approach

Axial spondyloarthritis (axSpA): Clinical features, diagnosis, and classification

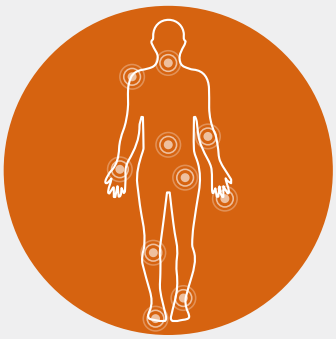
Axial spondyloarthritis (axSpA) is a chronic inflammatory condition affecting the spine and sacroiliac joints (SIJ) that connect the lower spine to the pelvis[1]

It manifests primarily as lower back pain, but can also affect other musculoskeletal and extra-musculoskeletal regions, thus making it a systemic inflammatory condition[1,2]

Chronic back pain due to axSpA can cause significant disability and impair the daily functions of affected individuals[1]

The long time span between disease onset and detection of clinical features on radiographs often delays diagnosis and treatment[3]

Clinical manifestations of axSpA[1,3]



- Inflammatory back pain
- Arthritis
- Enthesitis
- Dactylitis
- Uveitis
- Psoriasis

- Inflammatory bowel disease
- Good response to non-steroidal anti-inflammatory drugs (NSAIDs)
- Family history of SpA
- Human leukocyte antigen (HLA)-B27 positivity and elevated C-reactive protein

Diagnosis and classification of axSpA

Radiographic changes in the SIJ on X-ray were the established diagnostic criteria for radiographic-axSpA (traditionally known as ankylosing spondylitis)[1]

However, most young patients with short-duration symptoms show non-detectable substantial changes on radiographs termed as non-radiographic axSpA[1]

Magnetic resonance imaging (MRI) has emerged as a powerful tool for the early detection of SIJ and spinal inflammation in axSpA[3]

Classification criteria for patients diagnosed with axSpA developed by the Assessment of SpondyloArthritis international Society (ASAS)

For individuals with chronic low back pain (persisting for ≥3 months) starting at the age of ≤45 years old

Presence of sacroiliitis on imaging with at least one SpA feature[1,3]

HLA-B27 positivity with at least two SpA features[1]

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Pathogenesis, therapeutic targets, and treatment approaches

Primarily, individuals with a specific genetic makeup are more susceptible to developing axSpA, especially at the level of entheses and subchondral bone[4]

However, mechanical stress and inflammation also drive the progression of axSpA[4]

Hence, the signalling pathways of pro-inflammatory agents including IL-23/IL-17 and tumour necrosis factor (TNF)-α have been identified to play a key role in the inflammation and joint damage associated with axSpA[4]

Interleukin (IL)-17A, which belongs to the IL-17 family of cytokines, has been implicated in several autoimmune and inflammatory disorders[1,5]

Innate immune responses and inflammation mediated by IL-17A are pivotal in driving axSpA[1,5]

IL-17A

IL-17A blockade can serve as an effective treatment strategy for SpA[1,5]

Additional clinical data is needed to elucidate the molecular mechanisms underlying its role in enthesitis, pain, inflammation, bone formation, and bone erosion[5]

While IL-23 plays a key role in regulating IL-17 secretion and drives chronic inflammation in peripheral disease, agents that block IL-23 secretion were not effective for axSpA treatment. This indicates the possibility that the molecular mechanisms underlying axSpA pathogenesis might be independent of IL-23[1]

TNF-α is another key cytokine involved in axSpA pathogenesis. All TNF-α inhibitors have shown to be effective against SpA[3,5]

Downstream Janus kinase-signal transducer and activator of transcription (Jak-STAT) signalling cascade also regulates inflammation in axSpA. Hence, inhibitors of this pathway are effective for axSpA treatment[1]

Currently recommended treatment approaches for axSpA

Pharmacological interventions

NSAIDs[1]

If NSAIDS are ineffective: Biologics[1,3,6]

- TNF-α inhibitors: Adalimumab, certolizumab, etanercept, golimumab, and infliximab
- IL-17 inhibitors: Secukinumab and ixekizumab

If biologics are ineffective:

Re-evaluation of the diagnosis and consideration of the presence of comorbidities[1,3]

Switching to another biologic or Jak inhibitor is recommended[1,3]

Non-pharmacological interventions

Physical therapy[1,3]

Exercise[1,3]

Education (lifestyle)[3]

Treatment outcomes are assessed based on improvements in pain, stiffness, fatigue, motion, function, disease activity, and quality of life[3]

Treat to target approach for axSpA[3]

The rheumatologist, in consultation with the patient, should set up a treatment target defined as disease remission or alternatively as an inactive disease. This has the following advantages:

- Improved compliance and treatment adherence
- Long-term clinical benefits through optimal control of symptoms
- Enhanced patient–physician interactions and co-ordination between different specialists
- Increased systematic disease monitoring and adjustment of treatments

Treatment considerations for axSpA[3]

- Structural changes
- Functional impairment
- Extra-musculoskeletal manifestations
- Comorbidities
- Treatment risks

Emerging treatments for axSpA[1]

- Bimekizumab: Antibody that blocks IL-17A and F isoforms
- Intravenous secukinumab
- Namilumab: granulocyte-macrophage colony-stimulating factor (GM-CSF) blocking agent

Key barriers in the treatment of axSpA[1]

- Predicting the most appropriate medication for each patient
- Challenges in early detection of axSpA leading to delayed management

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Age and gender-related variations in the diagnosis and treatment of axSpA

Therapeutic management of late onset axSpA

While axSpA is highly prevalent in younger patients, an increase in the number of older patients with a late disease onset is possible, owing to a rise in the aging population[3]

Older patients often present with atypical clinical features, which are not detected through radiographs[3]

The onset of axSpA symptoms usually occurs at the age of ≥45 years in 3%–8% patients with the disease[3]

Recommendations for the diagnosis and treatment for radiographic axSpA are based on recommendations for younger patients and may not apply to an older population[3]

Clinical considerations for the management of late onset axSpA in older patients[3]

- Predominantly peripheral symptoms in older patients compared to axial symptoms in younger patients
- Extra-musculoskeletal manifestations due to a delay in diagnosis
- Aging-related complications
- Comorbidities
- Polymedication
- Changes in immune responses such as an increase in TNF-α levels
- Poor treatment response to conventional medication

Treatments for axSpA are based on recommendations for younger patients. Distinct clinical features of older patients must, therefore, be considered to improve diagnosis and treatment efficacy[6]

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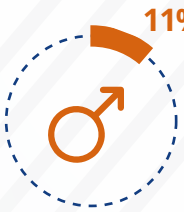
Gender-based variations in diagnosis, treatment outcomes, and health-related quality of life in patients with axSpA



Diagnostic delay and incorrect diagnosis of axSpA are more common in women (30%) than men (11%)[2]

This results in a greater number of visits and a higher probability of additional medical costs and unnecessary interventions[2]

Potential causative factors underlying gender-based variations[2]

Lack of awareness among women and poor communication with healthcare professionals

Under-representation of women in clinical trials

Social variables like education, occupation, family, and financial status

Lower treatment efficacy in women due to biological gender differences such as:

- Gene expression profile
- Inflammatory biomarkers
- Body and fat mass index

Recommended measures for the appropriate management of axSpA among female patients[2]

- Increasing disease awareness among female patients and healthcare professionals for improved disease management
- Identifying and addressing gender disparities in the diagnosis, clinical manifestations, and treatment outcomes due to biological differences
- Improving female representation in clinical trials

Future directions for the effective management of axSpA

Identifying patients with lower back pain who are at an increased risk of developing axSpA can aid their timely diagnosis[1]

Adopting individualised treatment approaches can guide the selection of appropriate treatments in a patient-specific manner[3]

Identification of novel biomarkers and therapeutic cellular targets that can be used for the detection of axSpA[1]

Collaborative approaches between primary clinicians, physiotherapists, and orthopedics can help bridge the gap between disease onset, diagnosis, and treatment[2]

Conclusions

- **Inclusion of MRI features in the diagnostic work-up has significantly improved the early detection of axSpA**
- **Diagnostic algorithm and classification criteria of axSpA are drawn from recommendations in younger patients and may, therefore, not be directly applicable to older patients**
- **Including older patients and women in clinical trials can improve their representation, thus, allowing the application of diagnostic and treatment approaches of axSpA across a larger patient population**

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