GRAPPA

Group for Research and Assessment of Psoriasis and Psoriatic Arthritis

Diagnosis & Assessment of Axial SpA

Dr. Mohamed Salah Eldin Abdel Baky

Prof. of Internal Medicine & Rheumatology

Ain Shams University Cairo Egypt

GRAPPA EGYPT 2024

Sponsored by NOVARTIS

GRAPPA
Group for Research and Assessment of Psoriasis and Psoriatic Arthritis

Disclosures

➢Speaker or advisory board member or clinical trials PI for:

- Abbvie
- Amgen
- Janssen
- Novartis
- Lilly
- Pfizer
- Organon
- Roche

GRAPPA
Group for Research and Assessment of Psoriasis and Psoriatic Arthritis

Key References

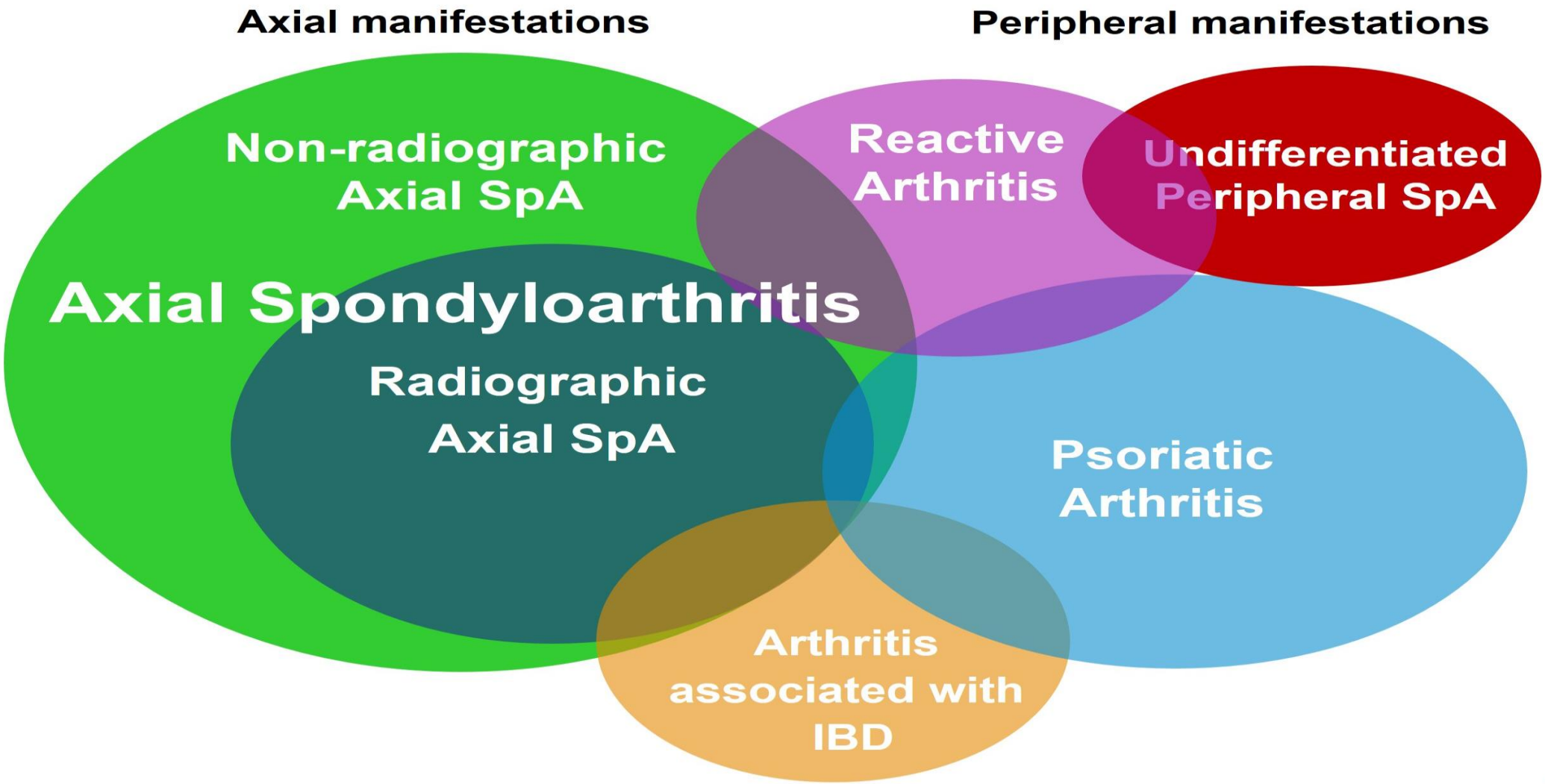
- Boel A, van Lunteren M, Lopez-Medina C, et al. RMD Open 2022;8(1)
- F.A. van Gaalen, M. Rudwaleit: Best Practice & Research Clinical Rheumatology 37 (2023) 101871
- Navarro-Compan. Axial Spondyloarthritis. Ann Rheum Dis 2021
- Protopopov M and Poddubnyy D, *Expert Rev Clin Immunol*. 2018;14:525–533.
- R obinson et al. Axial spondyloarthritis: concept, construct, classification and implications for therapy. Nat Rev Rheumatol 2021
- Rudwaleit M, van der Heijde D, Landewe R, et al. The development of Assessment of SpondyloArthritis international Society classification criteria for axial spondyloarthritis. Ann Rheum Dis 2009; 68(6):777e83.

GRAPPA
Group for Research and Assessment of

Objectives

- Classification of spondyloarthritis
- Axial spondyloarthritis (axSpA) clinical features
- Non-radiographic axSpA and radiographic axSpA
- ASAS classification criteria for Axial spondyloarthritis
- Parameters relevant for diagnosis
- Laboratory work-up
- Imaging
- Pitfalls in diagnosis of axial SpA
- Axial SpA assessment tools
- Conclusions

Classification of Spondyloarthritis

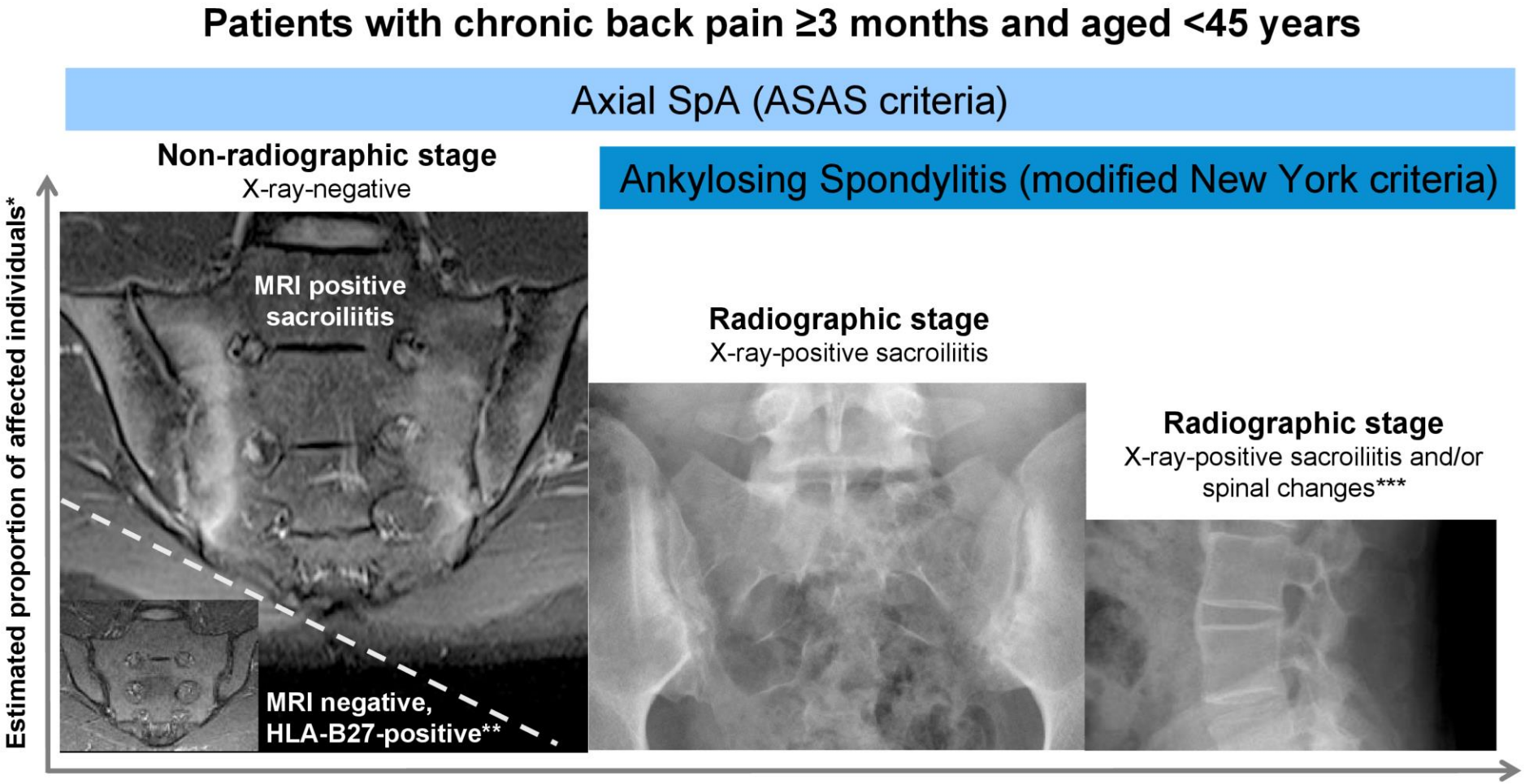


Modified from Proft F et al. Ther Adv Musculoskelet Dis 2018;10:129-39

Axial spondyloarthritis (axSpA)

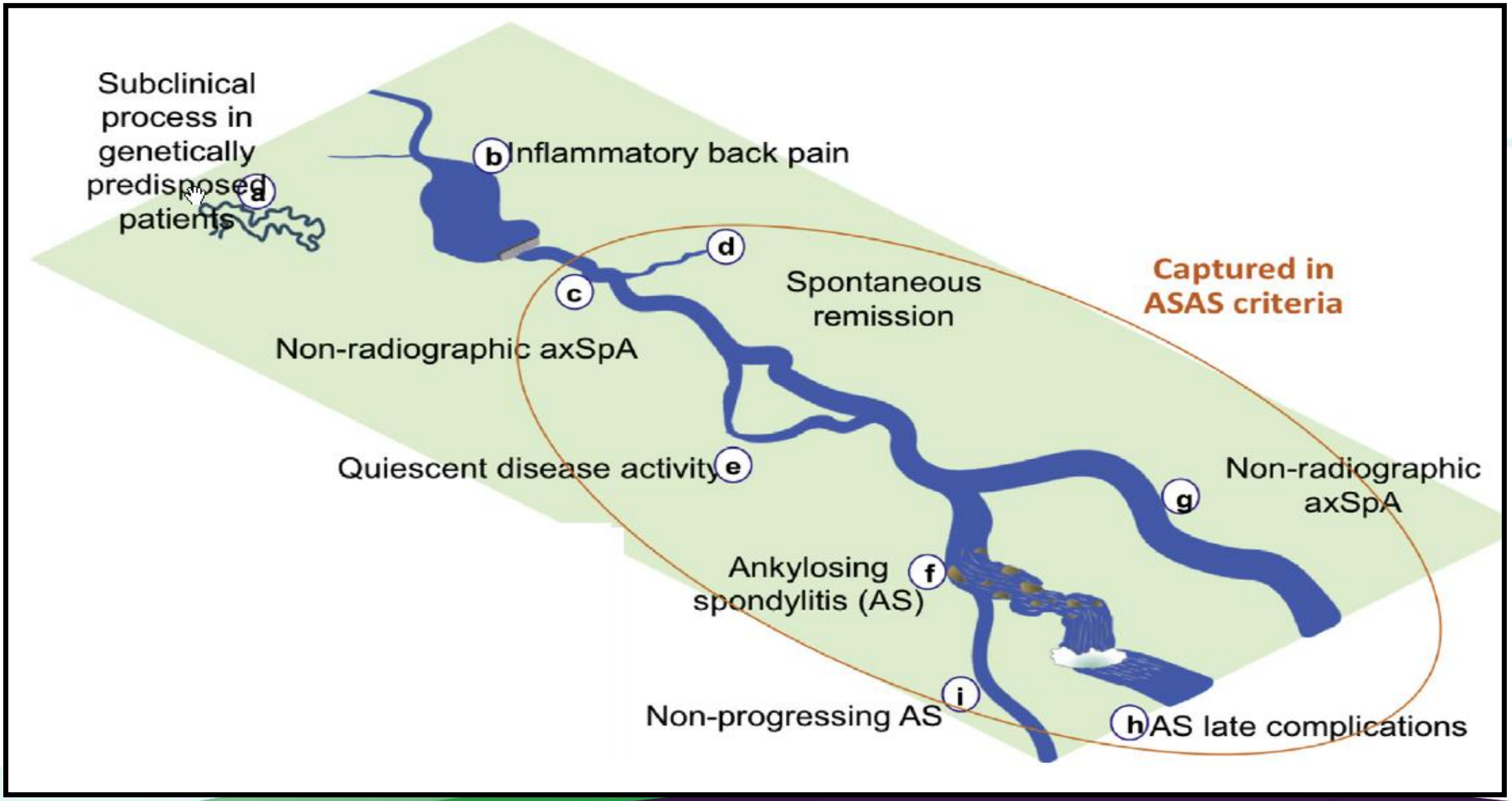
- Axial spondyloarthritis (axSpA) is a chronic inflammatory rheumatic disease that mainly affects the spine and sacroiliac (SI) joints.
- Peripheral manifestations (arthritis, enthesitis, and dactylitis)
- Extra-musculoskeletal manifestations (EMMs) (inflammatory bowel disease (IBD), psoriasis (PSO), and anterior uveitis (AU).

Axial spondyloarthritis (axSpA) is subdivided into **non-radiographic axSpA** (nr-axSpA) and **radiographic axSpA** (previously called ankylosing spondylitis)



* Heights reflect an estimate of the proportion of patients in each group
** Clinical arm if non-radiographic axial SpA
*** Radiographic evidence of inflammatory spinal changes including i.e., syndesmophytes, fusion or posterior element involvement

Sieper J et al. Arthritis Rheum 2013;65:543-51 (with permission)



Progression of Non-radiographic Axial SpA to radiographic Axial SpA (AS) German SpA Inception Cohort

Non-radiographic axial SpA

no definite radiographic sacroiliitis (grade 0 at the right side, grade 1 – possible subchondral sclerosis – at the left side)

12%
in 2 years

Main predictor:
elevated CRP**

Ankylosing spondylitis

definite radiographic sacroiliitis (grade 2 bilaterally) fulfilling the radiographic criterion of the modified New York criteria

*GESPIC = GErman Spondyloarthritis Inception Cohort

**Odds ratio for progression in patients with elevated serum C-reactive protein level (>6 mg/l) was: 4.11 (95% CI 1.13-14.95).

Poddubnyy D et al. Ann Rheum Dis 2011;70:1369-74

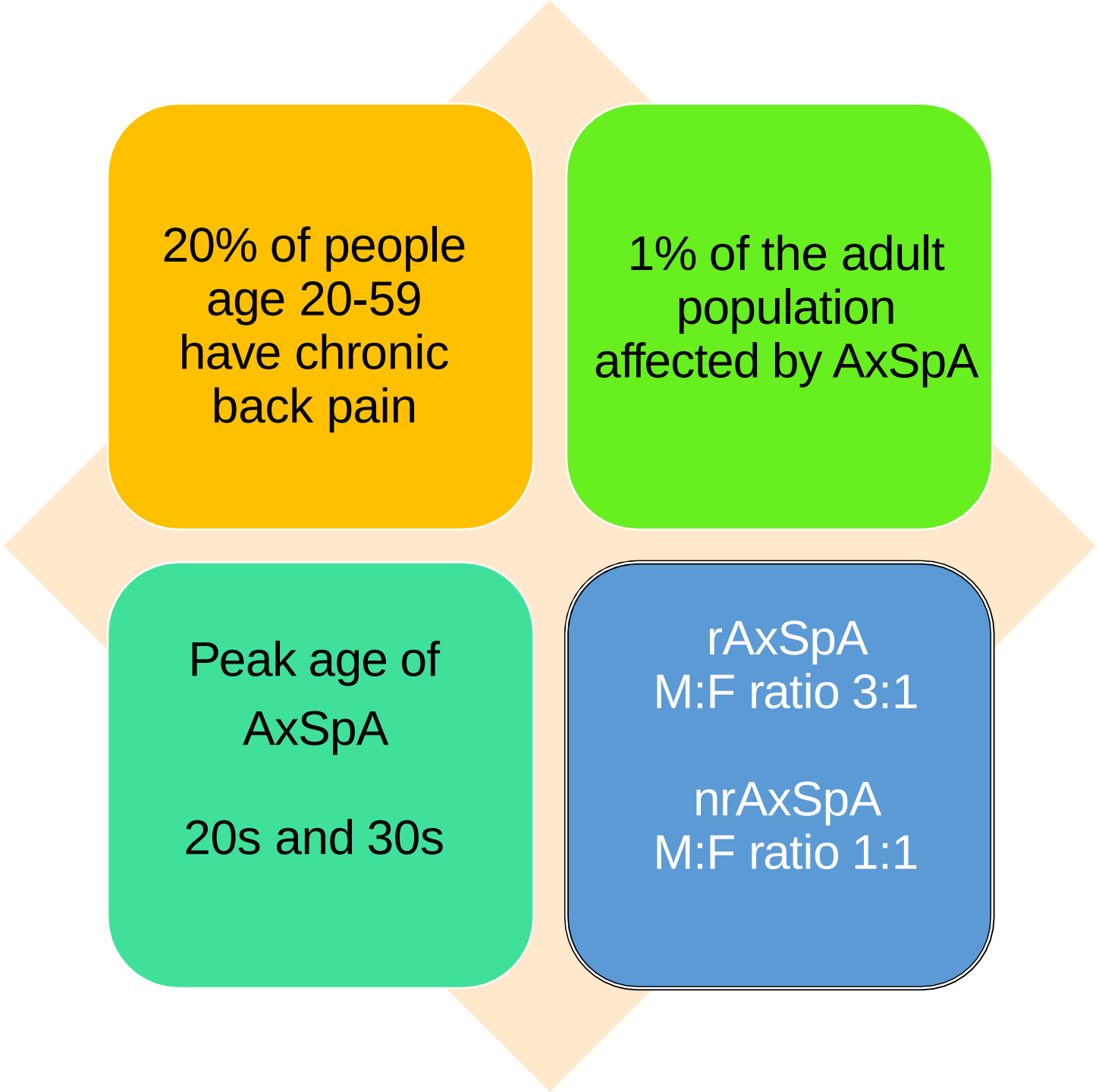
10 - 40% of patients with nr-axSpA progress to radiographic axSpA over a period of 2–10 years

Protopopov M and Poddubnyy D, *Expert Rev Clin Immunol*. 2018;14:525–533.

Risk factors for radiographic progression in nr-axSpA

- Genetic factors and protein markers
- HLA-B27 positivity
- Elevated CRP
- Structural changes on MRI
- Axial disease
- Buttock pain
- Male gender

1. Protopopov M and Poddubnyy D, *Expert Rev Clin Immunol*. 2018;14:525–533. 2. Malavviya AN, et al. *Int J Rheumatol*. 2017, Article ID 1824794. 3. Dougados M, et al. *Arthritis Rheumatol*. 2016;68(8):1904–. 2013;65:S1060–S1; 6. Dougados M, et al. *Ann Rheum Dis*. 2017;76(11):1823–8; 7. Jeong H, et al. *Int J Rheum Dis*. 2015;18(6):661–8; 8. Bochkova A, et al. *Ann Rheum Dis*. 2014;73(Suppl 2):439–40. 13; 4. Poddubnyy D, et al. *Ann Rheum Dis*. 2011:annrheumdis145995; 5. Haroon N, et al. Arthritis Rheum


20% of people age 20-59 have chronic back pain
1% of the adult population affected by AxSpA
Peak age of AxSpA
20s and 30s
rAxSpA
M:F ratio 3:1
nrAxSpA
M:F ratio 1:1

ASAS Classification Criteria for Axial Spondyloarthritis

In patients with ≥3 months back pain and age at onset <45 years

Sacroiliitis on imaging* plus ≥1 SpA feature	OR	HLA-B27 plus ≥2 other SpA features

*Sacroiliitis on imaging
- active (acute) inflammation on MRI highly suggestive of sacroiliitis associated with SpA
- definite radiographic sacroiliitis according to the modified New York criteria

SpA features:
- inflammatory back pain
- arthritis
- enthesitis (heel)
- uveitis
- dactylitis
- psoriasis
- Crohn's/colitis
- good response to NSAIDs
- family history for SpA
- HLA-B27
- elevated CRP

n=649 patients with back pain;

Overall
Sensitivity: 82.9%, Specificity: 84.4%
Imaging arm alone
Sensitivity: 66.2%, Specificity: 97.3%
Clinical arm alone
Sensitivity: 56.6%, Specificity: 83.3%

Rudwaleit M et al. Ann Rheum Dis 2009;68:777-783 (with permission)

ASAS

Ankylosing Spondylitis in the Pharaohs of ancient Egypt

Three pharaohs had ankylosing spondylitis:
Amenhotep II, Ramses II and his son **Merenptah**

Amenhotep II

X ray of the lumbar spine and upper pelvis of Amenhotep II: calcification of the paraspinous ligaments and obliteration of the sacroiliac joints

X ray of the lumbar spine and upper pelvis

Ernst Feldtkeller et al.Rheumatol Int (2003) 23: 1–5

Step-by-Step Diagnosis of Axial SpA

BMJ Best Practice. [Internet] [Updated Feb 28, 2017]. Available at: http://bestpractice.bmj.com/best-practice/monograph-pdf/366.pdf. Accessed on Oct 1, 2017.

Parameters Relevant for Diagnosis

Symptoms and history

Inflammatory back pain

Good response to NSAIDs

Asymmetric mono- und oligoarthritis

Enthesitis

Dactylitis

SpA family history

Preceding infection

Acute anterior uveitis

Psoriasis

Crohn / Ulcerative colitis

Inflammatory back pain

The most important clinical feature is inflammatory back pain (IBP)

- Age at onset < 40 year
- Insidious onset
- Improvement with exercise
- No improvement with rest
- Pain at night (with improvement on rising)

(At least four of five present)

IBP according to **ASAS** experts

J. Braun.. Clin Exp Rheumatol 2012; 30 (Suppl. 73): S132-S135.

It is important to differentiate between various types of back pain when diagnosing axial SpA

Features	Age	Onset	Characteristics	Physical activity	Morning stiffness	Inflammatory markers	Chronicity	Nocturnal pain	Location
Inflammatory back pain	<40 yrs	Insidious and persisting for >3 months	Alternating buttock pain Awakening due to back pain in the second half of the night	Improves with exercise	Moderate and persisting for >30–45 min	Elevated	>3 months	Commonly worse at night	Commonly back pain but may affect any part of the spine
Mechanical back pain	Any	Variable	Variable	Improves with rest	Mild and short-lived	Normal	Variable duration	Variable	Anywhere in the spine, may radiate to leg and numbness

axSpA, axial spondyloarthritis; IBP, inflammatory back pain; min, minutes

1. Strand V, Singh JA. *Mayo Clin Proc*. 2017;92:555–64; 2. Dillon CF, Hirsch R. *Am J Med Sci*. 2011;341:281–283;
3. Machado GC, et al. *Ann Rheum Dis*. 2017;76:1269–1278; 4. van der Heijde D, et al. *Ann Rheum Dis*. 2017;76:978–991..

Laboratory Work-up

- HLA-B27
- Acute phase response: CRP & ESR

Abbreviations: HLA, Human Leukocyte Antigen; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein;

Poddubnyy D. *Int J Clin Rheumtol*. 2011 Nov 22;6(6):655–67.

GRAPPA
Group for Research and Assessment of Psoriasis and Psoriatic Arthritis

HLA-B27

HLA-B27 is the most important single genetic risk factor for the disease.

The prevalence of HLA-B27 in the general population in Europe and North America is around 6 to 8% and about 2% to 5% among Arab populations.

The diagnostic value of HLA-B27 testing lies in the fact that HLA-B27 is consistently far more common in axSpA patients than in the general population.

90% of axSpA patients from Asia were HLA-B27 positive, 80% from Latin America,80% from Europe and North America and 65% from Middle East and North Africa.

Boel A, van Lunteren M, Lopez-Medina C, et al. RMD Open 2022;8(1)
Khader N. Mustafa, M. Hammoudeh, M. Khan.
Journal of Rheumatology August 2012

GRAPPA
Group for Research and Assessment of Psoriasis and Psoriatic Arthritis

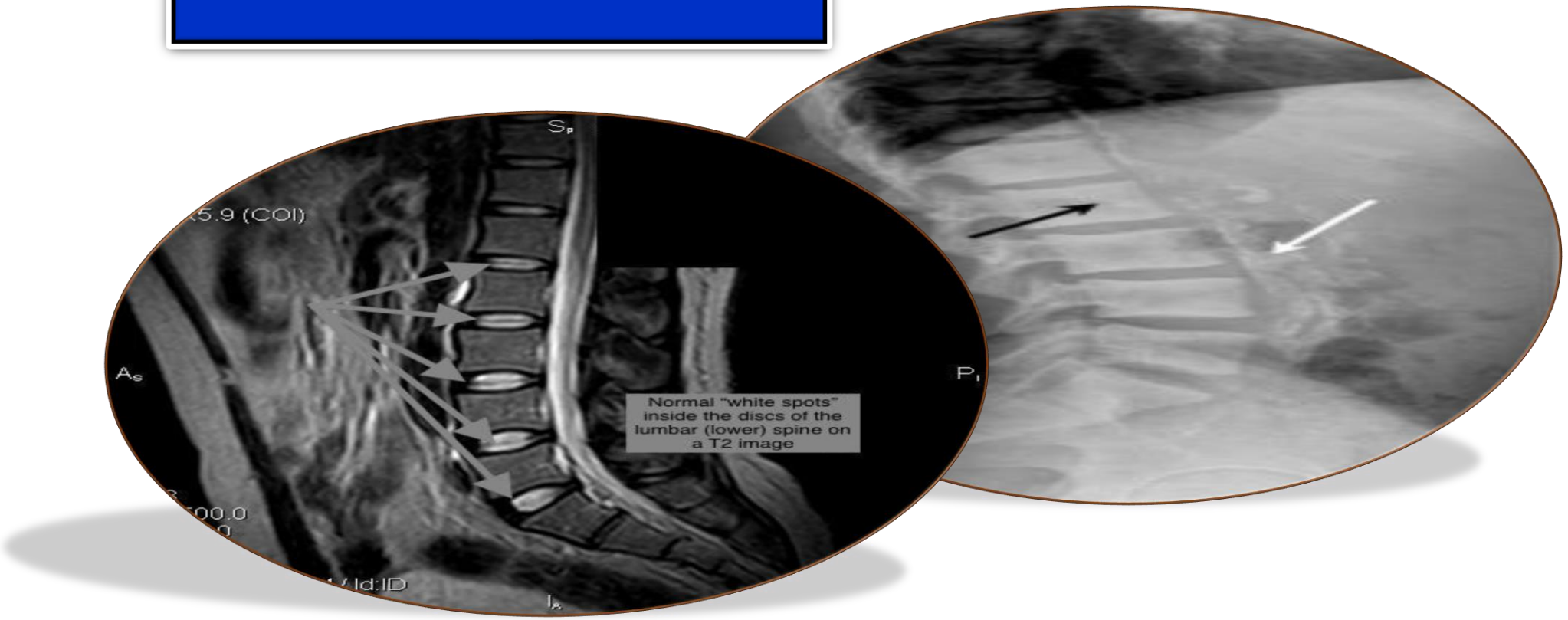
Why the CRP

- Increased CRP was frequently observed in patients with painful axial AS and was correlated both with activity and functional severity of the disease.
- Elevated C-reactive protein (CRP) levels are associated with radiographic sacroiliitis progression in (AS) patients.
- CRP, in addition to patient-reported and clinical outcomes, might be useful to help monitor response to treatments.
- Elevated CRP levels are observed in about 25 - 40% of patients with axSpA.

Rudwaleit M, Haibel H, Baraliakos X, et al. Rheum 2009;60(3):717e27.

GRAPPA
Group for Research and Assessment of Psoriasis and Psoriatic Arthritis

IMAGING



GRAPPA
Group for Research and Assessment of Psoriasis and Psoriatic Arthritis

Grading of Radiographic Sacroiliitis

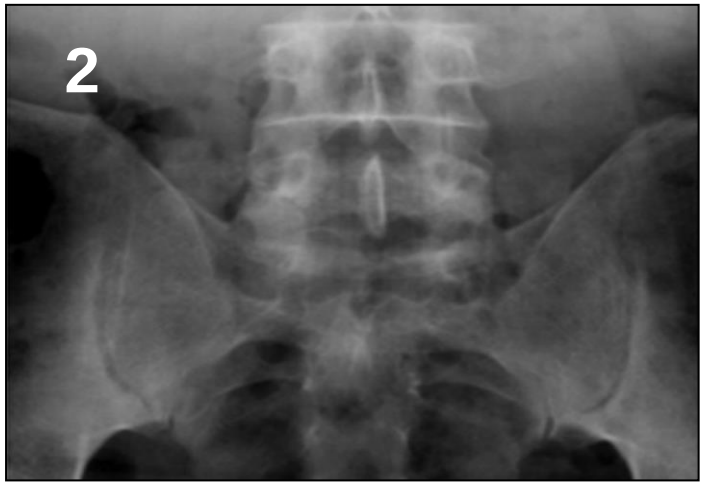
- **Grade 0** normal
- **Grade 1** suspicious changes
- **Grade 2** minimal abnormality – small localized areas with erosion or sclerosis, without alteration in the joint width
- **Grade 3** unequivocal abnormality – moderate or advanced sacroiliitis with one or more of: erosions, evidence of sclerosis, widening, narrowing, or partial ankylosis
- **Grade 4** severe abnormality – total ankylosis

Bennett PH, Burch TA: Amsterdam.Excerpta Medica Foundation International Congress Series 148, 1966:456-457

ASAS

GRAPPA
Group for Research and Assessment of Psoriasis and Psoriatic Arthritis

Grading of Radiographic Sacroiliitis

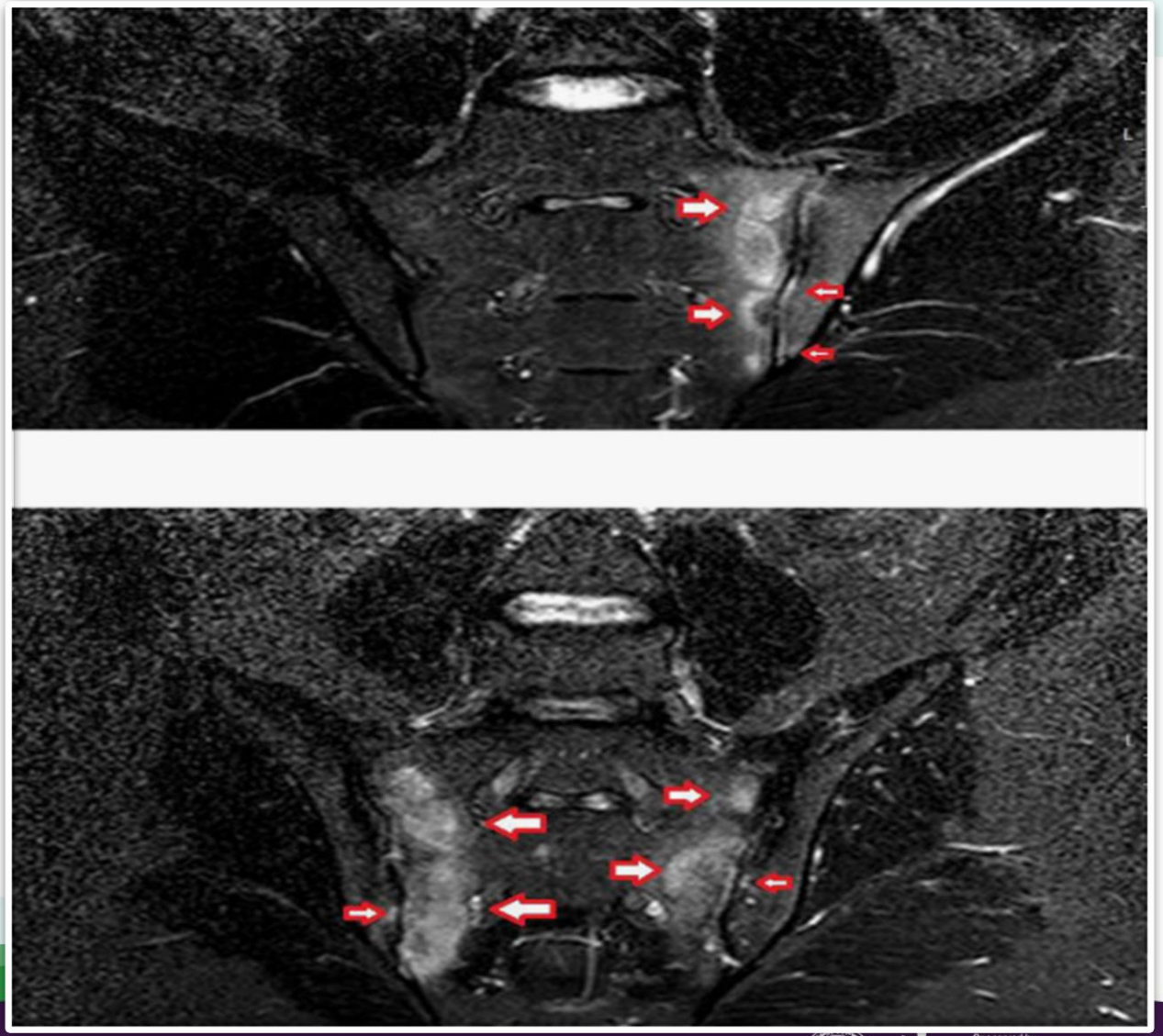


Sponsored by NOVARTIS

MRI-SI Joint

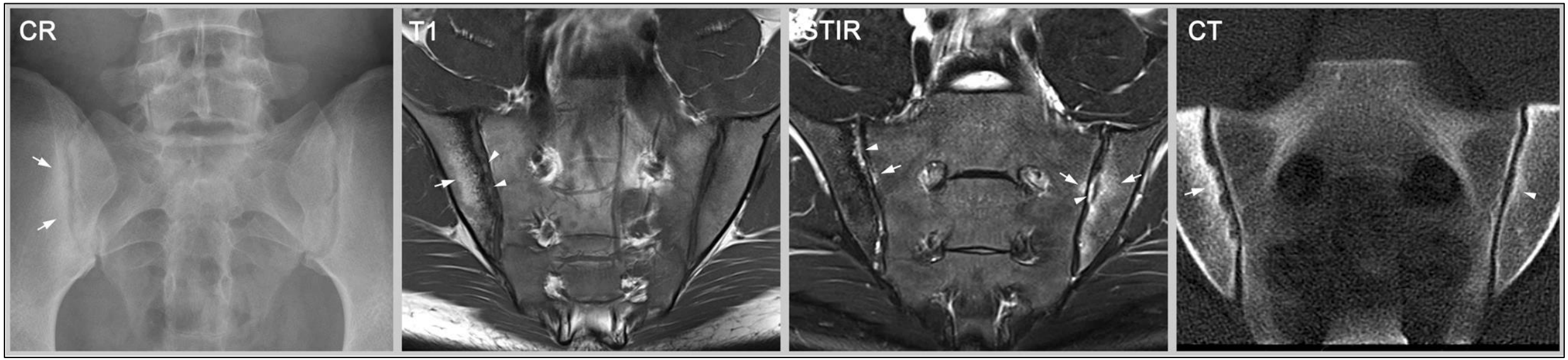
Unilateral bone-marrow edema in the left sacroiliac joint.

Bilateral bone-marrow edema in the sacroiliac joints.



GRAPPA
Group for Research and Assessment of Psoriasis and Psoriatic Arthritis

Sacroiliitis imaging typical findings for axSpA

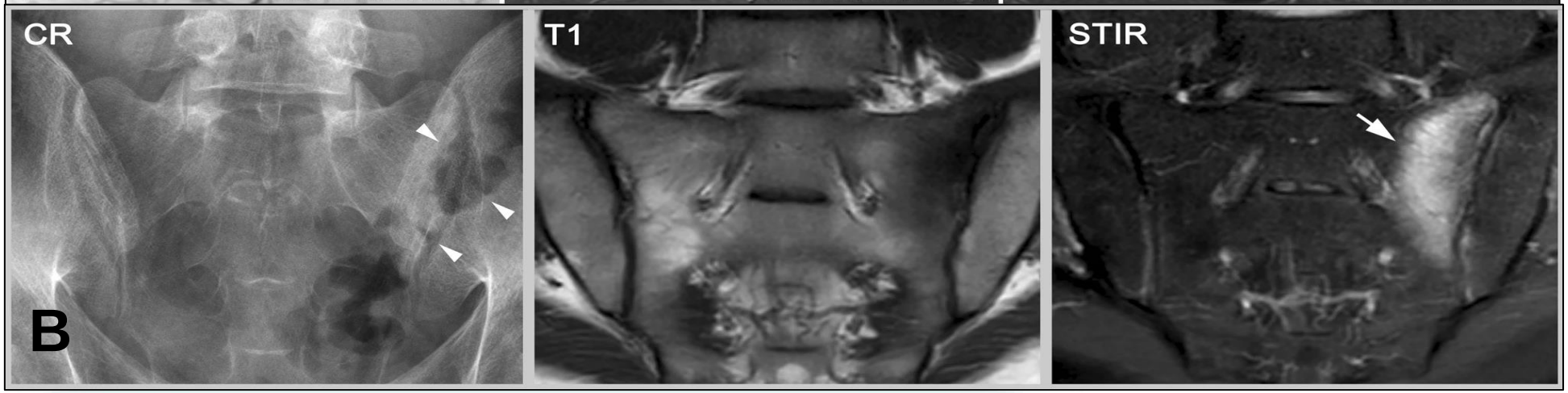


sclerosis and erosions	fatty marrow metaplasia and erosion	inflammatory bone marrow lesions	erosions and sclerosis with high resolution

Differential diagnosis of BME at the sacroiliac joint

A. pregnancy/ childbirth bone marrow edema (BME)

B. stress fracture of the left sacrum in a patient with extensive sporting activities



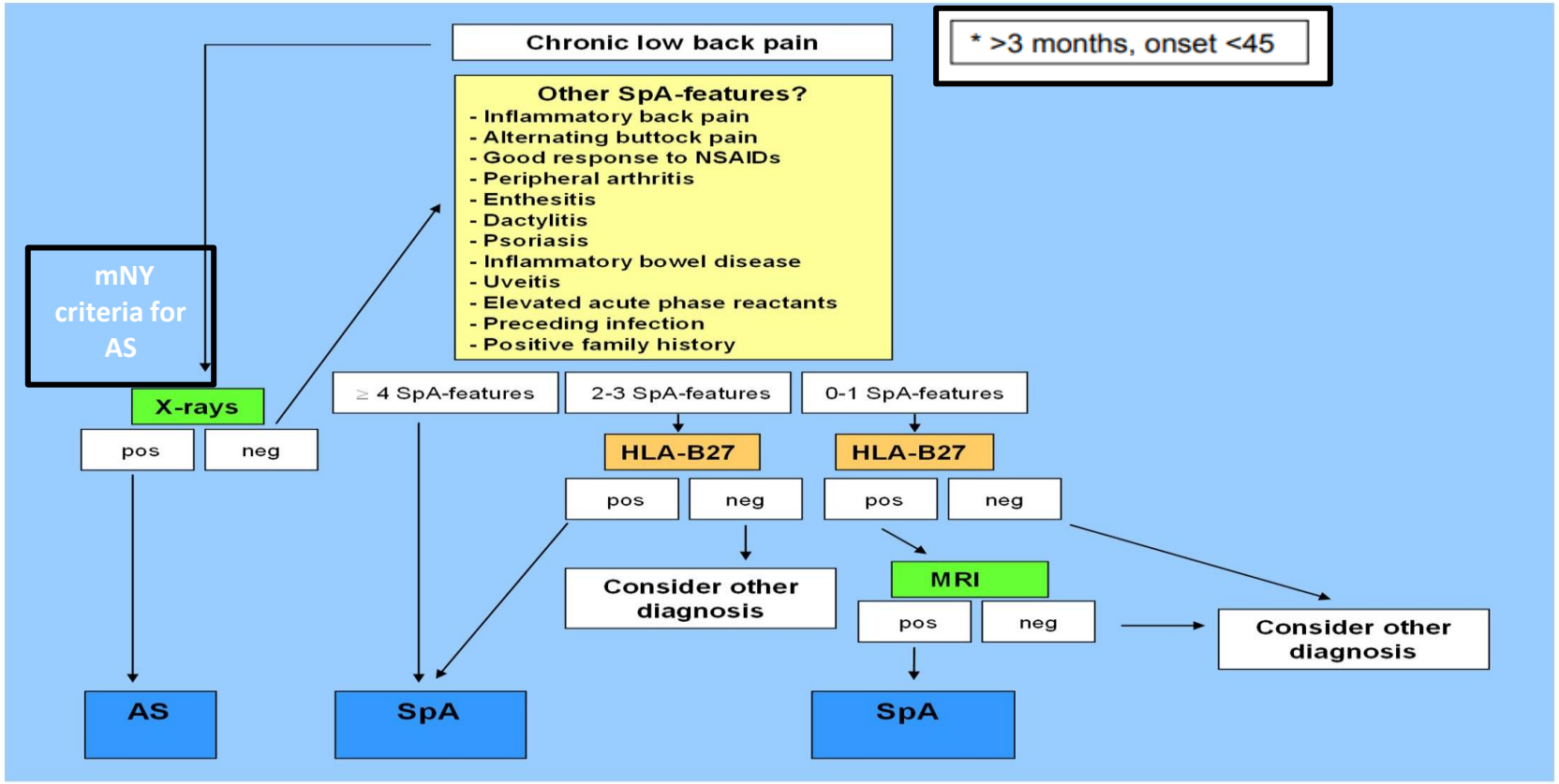
Kiil RM et al. Arthritis & Rheumatology Vol. 0, No. 0, Jan 26 2023 pp 1–10

GRAPPA
Group for Research and Assessment of Psoriasis and Psoriatic Arthritis

Low Dose CT

Low Dose CT of the sacroiliac joints in AS
areas with erosions and sclerosis

ASAS Modification of the Berlin Algorithm for Diagnosing Axial SpA



Adapted from: van den Berg R et al. Ann Rheum Dis 2013;72:1646-53 (with permission)
*Rudwaleit M et al. Ann Rheum Dis 2004;63:535-43

ASAS

Sponsored by NOVARTIS

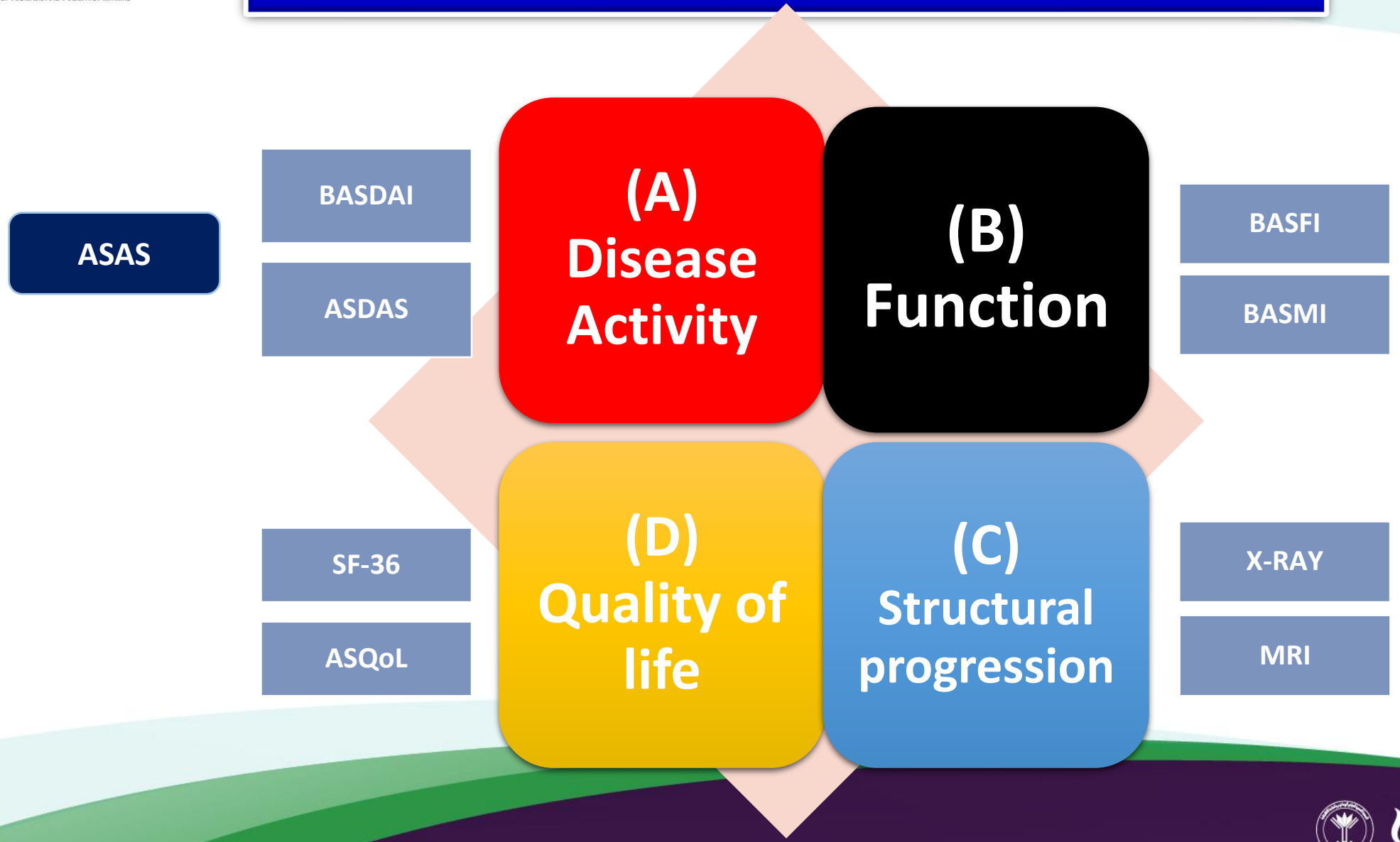
Pitfalls in Diagnosis of Axial SpA

1. **Using classification criteria for diagnosis:** not only ignores the important issue of differential diagnosis but also leads to an unacceptable number of misdiagnoses both on axSpA patients incorrectly not diagnosed (due to too low sensitivity for diagnosis 82%) and patients without axSpA incorrectly diagnosed as axSpA (due to too low specificity for diagnosis 87%).
2. **Diagnosis by simply adding up SpA features:** the risk of overdiagnosis of axSpA when the diagnosis is made by simply counting the number of SpA features without clinical reasoning and without paying attention to an alternative diagnosis that may better explain the symptoms. The ASAS-modified Berlin algorithm is only a tool in aiding rheumatologists in diagnosing axSpA and should not replace a differential diagnostic procedure in patients with CBP.
3. **Misinterpretation of imaging findings:** MRI findings of BME alone are not necessarily diagnostic of axSpA and MRI should always be interpreted in the context of other clinical and laboratory findings. other causes of bone BME in the SI joints such as mechanical stress should always be considered.

F.A. van Gaalen, M. Rudwaleit Best Practice & Research Clinical Rheumatology 37 (2023) 101871

GRAPPA
Group for Research and Assessment of Psoriasis and Psoriatic Arthritis

Axial SpA Assessment Tools



Bath Ankylosing Spondylitis Activity Index
A BASDAI score >4 indicate Active Disease

Bath Ankylosing Spondylitis Disease Activity Index (BASDAI)

Items to be scored by the patient:

1. How would you describe the overall level of fatigue/tiredness you have experienced?
2. How would you describe the overall level of AS back, neck or hip pain you have had?
3. How would you describe the overall level of pain/swelling in joints other than back, neck, hips you have had?
4. How would you describe the level of discomfort you have had from an area tender to touch or pressure?
5. How would you describe the level of morning stiffness you have had from the time you wake up?
6. How long does the morning stiffness last from the time you wake up?

Garrett S et al. J Rheumatol 1994;21:2286-91

ASAS

How /What is it assessed?

6 questions assessing the following (over the previous week), using a visual analog scale (0–100 mm) or numerical rating system (0–10):

- **Fatigue**
- **Spinal pain**
- **Peripheral arthritis**
- **Enthesitis**
- **Intensity and duration of morning stiffness**

What does it mean?

- **Higher scores = worse disease activity**
- **A BASDAI score >4 indicate active disease**

Axial Spondyloarthritis Disease Activity Score (ASDAS)

Ankylosing Spondylitis Disease Activity Score (ASDAS)

Parameters used for the calculation of the ASDAS

1. Total back pain (BASDAI question 2)
2. Duration of morning stiffness (BASDAI question 6)
3. Patient global assessment of disease activity
4. Peripheral pain/swelling (BASDAI question 3)
5. C-reactive protein (CRP) in mg/l [or erythrocyte sedimentation rate (ESR)]

Lukas C et al. Ann Rheum Dis 2009;68:18-24 (with permission)
van der Heijde D et al. Ann Rheum Dis 2009;68:1811-8 (with permission)

ASAS

Cut-offs for disease activity states and disease improvement scores

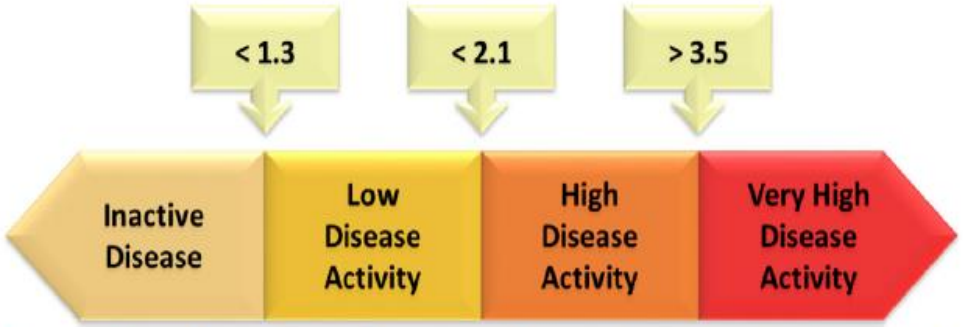
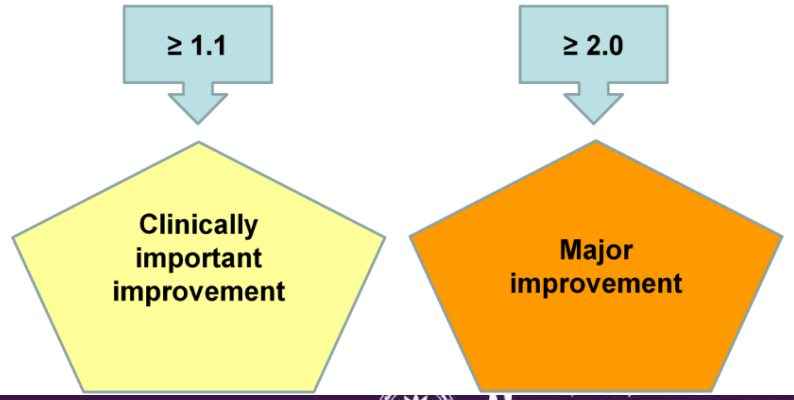


Figure 1 2018 update of the nomenclature for Ankylosing Spondylitis Disease Activity Score (ASDAS) disease activity states.



Ann Rheum Dis 2009;68:1811–1818. doi:10.1136/ard.2008.100826

NOVARTIS

Bath Ankylosing Spondylitis Functional Index (BASFI)

Items to be scored by the patient:

1) Putting on your socks or tights without help or aids (eg, sock aid).
2) Bending forward from the waist to pick up a pen from the floor without an aid.
3) Reaching up to a high shelf without help or aids (eg, helping hand).
4) Getting up out of an armless dining room chair without using your hands or any other help.
5) Getting up off the floor without help from lying on your back.
6) Standing unsupported for 10 min without discomfort.
7) Climbing 12 to 15 steps without using a handrail or walking aid. One foot at each step.
8) Looking over your shoulder without turning your body.
9) Doing physically demanding activities (e g, physiotherapy, exercises, gardening or sports).
10) Doing a full day's activities, whether it be at home or at work.

The BASFI is the mean of 10 item scores completed on a numerical rating scale

How is it assessed?

- 8 questions regarding function in AS
- 2 questions reflecting the patient's ability to cope with everyday life
- Scored on a visual analog scale (0–100 mm)

What does it mean?

Higher scores = worse functional impairment

Bath Ankylosing Spondylitis Metrology Score (BASMI)

i. **The BASMI comprises four spinal measurements**
   1. Cervical rotation
   2. Tragus-to-wall distance
   3. Modified Schober's test
   4. Lumbar lateral flexion

ii. **One hip mobility measurement**
   5. Intermalleolar distance

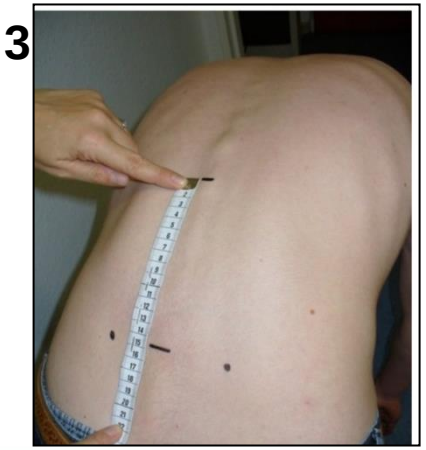
What does it mean?

- The higher the BASMI score the more severe the patient's limitation of movement due to their AS

1

2

3



4

5

Moncur C. *Arthr Rheum.* 2003,49:197–209

GRAPPA
Group for Research and Assessment of Psoriasis and Psoriatic Arthritis

Conclusions

- Diagnosis of axial spondyloarthritis (axSpA) with no pathognomonic feature, remains a skill that involves the recognition of a pattern of features that taken together provide sufficient evidence to diagnose the disease.
- Patient history, physical examination, and selected laboratory (HLA-B27, CRP), and imaging studies are used in diagnosing ax SpA.
- Conditions that cause chronic spinal and low back symptoms may present in a similar way to ax SpA and should be ruled out before making a diagnosis.
- Diagnostic pitfalls such as using classification criteria as diagnostic criteria, making a diagnosis by simply adding up SpA features or misinterpretation of imaging must be avoided.

GRAPPA

Group for Research and Assessment of Psoriasis and Psoriatic Arthritis

THANK YOU!