The gestalt of spondyloarthritis: From early recognition to long-term imaging outcomes

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Chapter 5

Five-year follow-up of radiographic sacroiliitis: progression as well as improvement?

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Determining the presence of radiographic sacroiliitis is a key feature in the diagnostic process of radiographic axial spondyloarthritis (r-axSpA), synonymous to ankylosing spondylitis according to the modified New York criteria (mNY).[1] Its presence is considered prognostically relevant and paves the way for treatment with biological drugs.[2] Multiread and multireader exercises have proven that radiographic sacroiliitis is an ambiguous finding, as reflected by large inter-reader and intrareader variability.[3, 4]

Determining *progression* of radiographic sacroiliitis, which marks the arbitrary but irreversible change from non-radiographic axSpA (nr-axSpA) to r-axSpA, is even more ambiguous. The mNY lack sensitivity-to-change in this slowly progressing condition, and it is conceivable that *regression* of radiographic sacroiliitis is very rare if not impossible.[5] Previous studies addressing progression from nr-axSpA to r-axSpA have ignored regression and have only interpreted progression.[6] However, from a methodological perspective, bi-directional change cannot be ignored.

The aim of this study was therefore to assess positive and negative changes on plain pelvic radiographs (X-SI) over time in the Assessment of SpondyloArthritis international Society (ASAS)-cohort, in which X-SI judgements have been provided by single local readers from many centres worldwide.

In the ASAS cohort, 975 patients with either chronic back pain (>3 months, onset <45 years) of unknown origin or undiagnosed peripheral symptoms were assessed at baseline.[7, 8] Of these, 564 patients were reassessed after a mean follow-up of 4.4 years (range: 1.9-6.8). Patients with paired X-SI available (at baseline and follow-up) were included and judgements of the local observer (rheumatologist/radiologist) at both time points (either by the same or other reader) were analysed. Positive cases were defined as definite radiographic sacroiliitis according to the mNY.

In total, 357 patients had paired X-SI available. Of these, 17.4% (62/357) fulfilled the criteria for r-axSpA (table 1). At follow-up this proportion has raised to 22.4% (80/357) suggesting a net-progression of 5%. Cross-tabulation, however, revealed that more than half (36/62) considered mNY-positive at baseline were assessed mNY-negative at follow-up (table 2). If true, this would mean that radiographic sacroiliitis would have regressed in 58% of the cases. Conversely, only 54/295 patients (18.3%) became positive at follow-up.

It is very difficult to interpret these data, since progression, regression and measurement error (leading to spurious change) cannot be disentangled. Under the untenable assumption of 'no true change', the kappa statistic would yield a very poor figure of 0.21 (only marginally better than chance-agreement), which would make it useless from a diagnostic perspective.

If only positive change (progression) is valued and negative change is ignored, one would disregard measurement error and spuriously attribute part of the observed positive change to real progression.

The most likely explanation of our strange and extreme observation is that subtle radiographic progression (the signal) – if truly present – cannot be reliably distinguished from measurement error (the noise). These sobering data clearly illustrates that more research is needed in visualising progression in axSpA. Imaging modalities other than radiographs should be evaluated in future such as MRI and low-dose CT.

Table 1. Baseline characteristics of patients with baseline and follow-up pelvic radiographs

	Patients with paired radiographs (N=357)
Age, years (mean, SD)	33.8 (10.8)
Age at onset of back pain, years (mean, SD)	26.2 (8.8)
Male gender, n (%)	171 (47.9)
Number of SpA features* (mean, SD)	2.5 (1.4)
Definite radiographic sacroiliitis (mNY), n (%)	62 (17.4)
Active inflammation of SIJ¥, MRI, n (%) (n=223)	112 (50.2)
HLA-B27 positivity, n (%)	174 (48.7)
Elevated CRP, n (%)	135 (37.8)
IBP (According to experts definition), n (%)	178 (49.9)
Peripheral arthritis past or present, n (%)	193 (54.1)
Heel enthesitis past or present, n (%)	79 (22.1)
Uveitis past or present, n (%)	32 (9.0)
Dactylitis past or present, n (%)	39 (10.9)
Psoriasis past or present, n (%)	27 (7.6)
IBD past or present, n (%)	14 (3.9)
Good response to NSAIDs, n (%)	126 (35.4)
Family history of SpA, n (%)	79 (22.1)
Preceding infection, n (%)	11 (3.1)
Schober's test (cm), mean (SD) (n=354)	4.4 (2.5)
Chest expansion (cm), mean (SD) (n=351)	5.6 (5.7)
Active inflammation of the spine¥, MRI, n (%) (n=110)	29 (26.4)

* Features included: Inflammatory back pain (IBP), arthritis, heel enthesitis, dactylitis, uveitis, psoriasis, inflammatory bowel disease (IBD), good response to NSAIDs, family history of spondyloarthritis, elevated CRP. ¥ Presence or absence of typical signs of active inflammation independent of formal criteria. SIJ, sacroiliac joints; SpA, spondyloarthritis; mNY, modified New York criteria; MRI, magnetic resonance imaging.

Table 2. Radiographic sacroiliitis according to the modified New York criteria at baseline and at follow-up (on average 4.4 years)

	Follow-up radiograph		
Baseline radiograph	Positive	Negative	**Total**
Positive	26	36	**62**
Negative	54	241	**295**
Total	**80**	**277**	**357**
PPV (%)	41.9		
NPV (%)	81.7		

PPV, positive predictive value; NPV, negative predictive value.

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