

Ankylosing Spondylitis: What Do We Really Know About the Onset and Progression of This Disease?



Ankylosing spondylitis (AS) is a chronic inflammatory disease characterized by spinal pain and stiffness. It affects mainly the sacroiliac joints and the axial skeleton, leading to bony ankylosis. Peripheral arthritis, especially of the hips and shoulders, and extraarticular features such as acute anterior uveitis, aortitis, and pulmonary fibrosis of the upper lobes can be present as well. According to the modified New York criteria¹ sacroiliitis is the hallmark of the disease and a prerequisite for establishment of the diagnosis. It is supposed that it takes a long time before radiographic evidence of sacroiliitis is present, and, thus, before definite AS can be diagnosed. In addition, judgment regarding the radiographic presence of sacroiliitis can be quite difficult. In a recent study scoring of sacroiliac joints showed a worse intraobserver and a moderate interobserver reliability when different scoring methods were applied².

The International Ankylosing Spondylitis Working Group has developed core sets for the assessment of AS^{3,4}, defining separate core sets for different treatment settings, i.e., symptomatic therapy, disease modification, physiotherapy, and clinical practice. Two radiographic scoring methods, the Bath Ankylosing Spondylitis Radiology Index (BASRI) and the Stoke Ankylosing Spondylitis Spine Score (SASSS), are available. Both have showed good and excellent reliability, respectively, in defining structural damages to the spine in AS². The BASRI is a global grading system (grades 0–4) and consists of BASRI_s for the spine only, BASRI_h for the hips only, and BASRI_t for the sum of both^{5,6}. The modified version of the SASSS proved to be more reliable in comparing reliability and sensitivity in one year followup compared to the BASRI². In the plenary session of the OMERACT in 1998 both methods were judged as feasible methods⁷. However, no method could pass the test of the OMERACT filter for truth and discrimination, and both instruments should be the object of future studies⁷.

Longitudinal studies in AS are scarce, and most are cross sectional studies with a low frequency of assessments in patients or additionally with retrospective data collection of radiographs. The numbers of studied patients are small and the disease duration at start of the study is often high. Until recently no radiographic scoring system for AS was available, and, thus, most studies present their radiographic features in a descriptive manner. Nonetheless, they present valuable data as presented in Table 1. In a prospective study of 51 AS patients with a mean disease duration of 38 years there seemed to be a predictable pattern emerging in the first 10 years of disease¹³: 74% of the patients who had mild spinal restriction after 10 years did not progress to more severe restriction, and 81% of the patients who had severe spinal restriction were severely restricted within the first 10 years; moreover, hips that were normal after 10 years of disease did not become diseased subsequently. Recently it was found that hip disease was a major prognostic marker for longterm severe disease and that hip involvement was more prevalent in patients with a young age of onset¹⁴. In the future longitudinal studies using retrospective data will be more difficult to interpret since the median age of onset of symptoms steadily increased in the last century¹⁵, possibly leading to cohort effects.

Due to the lack of prospective longitudinal studies in early AS, a lot about prognostic factors, disease progression, and the rate of progression remains unknown.

This issue of *The Journal* features a cross sectional study of AS patients in whom radiographs were scored retrospectively using the BASRI¹⁶. Progression of the disease and rate of progression of radiological changes were calculated in subgroups of patients. Backward extrapolation of these results, if progression is supposed to show linearity, suggests the approximate time of first radiological change of the sacroiliac joint should be at age 8 years. Again, this study, like the others discussed before, contains cross

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Table 1. Radiographic features in longitudinal studies in AS⁸⁻¹².

	Spencer ⁸ 1979	Marks ⁹ 1983	Eustace ¹⁰ 1993	Gran ¹¹ 1997	Lee ^{*12} 2001
No. of patients	200	50	83	100	181
Study type	Cross sectional	Retrospective	Prospective and retrospective	Retrospective	Prospective
Disease duration (mean, yrs)	17.2	18.9	16.5	16.6	11.0
Radiographs (%)					
Cervical spine involvement	NA	} 35:24 [†] 71:29 [†]	11	56	40.3
Lumbar spine involvement	NA		42	59	NA
Syndesmophytes	64	—	—	—	—
Bamboospine	11.5	—	—	—	—

* The only study using a radiographic scoring method. † Female:male.

sectional data, making interpretation of the results difficult. In addition, the suspected linearity, which has not been observed before, is difficult to prove, especially since the onset of the sacroiliitis is unknown and not documented in early AS using techniques other than conventional radiography. It might be speculated that the rate of progression is not linear, but s-shaped or staircase-like. Disease activity was not documented, so it is not possible to analyze a correlation between disease activity and the occurrence of damage as reflected in radiographic progression. It would be very interesting to learn more about the disease activity over a determined period and the subsequent radiographic progression. This is of special interest because it is not known whether some changes correspond with healing and do not reflect damage, a topic that was discussed during the OMERACT plenary session⁷. Nonetheless this paper contains very interesting data and hypotheses, which are inviting for future studies, especially if the disease or radiographic changes in the sacroiliac joint start at such a young age.

This supposed young age of onset of sacroiliac changes once more stresses the need for development and validation of methods for early diagnosis of sacroiliitis, which ideally should then be added to the diagnostic criteria of AS. Over the last decade computer tomography (CT) and magnetic resonance imaging (MRI) were studied extensively in the diagnosis of AS. CT was proven to be a very good method to demonstrate already established bony changes. MRI has the advantage of combining good visualization of the complicated anatomy of the sacroiliac joint with the ability to localize different degrees of inflammation and edema¹⁷. Different MRI techniques were studied, like the fat suppression technique, SPIR and dynamic gadolinium enhancement. The latter technique seemed to be most promising in showing detailed enhancement, which could be quantified in the sacroiliac joint, the surrounding bone

marrow, and the joint capsule. This enhancement diminished after successful therapy¹⁷, making this technique a possible method for evaluation of treatment effects. Another advantage of MRI is its usefulness as a diagnostic tool in children, being a less harmful technique than conventional radiography and CT, and seemingly a technique that enhances detection of sacroiliitis in children with spondyloarthropathies¹⁸.

Disease modifying treatment of AS has been reviewed extensively¹⁹; however, there have been only a small number of randomized double blind controlled trials, and only sulfasalazine was studied in sufficient detail to allow definitive conclusions. Sulfasalazine was found to be an effective drug, especially in a subgroup of AS patients with peripheral arthritis. In view of treatment with infliximab over the last 2 years, this monoclonal chimeric tumor necrosis factor- α (TNF- α) antibody appears to truly be a disease modifying drug: it showed both efficacy in peripheral arthritis and significant improvement in clinimetric scores of the axial skeleton in 2 open studies^{20,21}. Imaging of the axial skeleton showed improvement even in advanced disease, which was a very surprising result.

These favorable results of anti-TNF treatment in AS and the suspected early age of onset of radiographic changes in the sacroiliac joints emphasize the need for: (1) diagnosis of early sacroiliitis; (2) development and validation of MRI for the detection of early sacroiliitis and subsequent addition to diagnostic criteria; (3) longitudinal prospective studies using the core sets as proposed by the OMERACT in early AS, in order to lift more than a tip of the veil of this disease. Possible investigations include prognostic factors, subgroups of patients prone to having a severe disease, pathogenetic mechanisms, and the relationship between disease activity and radiographic abnormalities, i.e., which changes correspond to damage and which correspond to healing, if healing occurs; and (4) additional studies with

anti-TNF and perhaps other “biologics” in AS in order to prove their efficacy, safety, and disease modifying properties.

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