

MRI in predicting a major clinical response to anti-tumour necrosis factor treatment in ankylosing spondylitis

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ABSTRACT

Objective: To evaluate the role of MRI in predicting a Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) improvement of at least 50% (BASDAI 50) upon anti-tumour necrosis factor (TNF) therapy of active ankylosing spondylitis (AS).

Methods: MRIs from patients with active AS who participated in randomised controlled trials were analysed with respect to presence and extent of active inflammatory lesions as detected in the spine (n = 46), sacroiliac (SI) joints (n = 42) and both sites (n = 26). Univariate and multivariate logistic regression analyses were applied to evaluate MRI and clinical data in predicting a BASDAI 50 response.

Results: The Berlin MRI spine score (odds ratio (OR) 1.16, 95% CI 1.02 to 1.33) and disease duration (OR 0.9, 95% CI 0.63 to 0.97) were statistically significant predictors of a BASDAI 50 response using regression analysis while there was only a trend for C-reactive protein (CRP). The likelihood ratio (LR) for achievement of BASDAI 50 was increased in patients with a Berlin MRI spine score ≥ 11 (LR 6.7), disease duration < 10 years (LR 4.2) and CRP ≥ 40 mg/litre (LR 3.4). All patients with two or three of these predictors improved clinically (as assessed by BASDAI) by at least 45%. Disease duration > 20 years, normal CRP and no active inflammatory lesion in the spine were highly predictive of not achieving BASDAI 50. A trend was only found for the MRI score of SI joints to be predictive.

Conclusions: Widespread inflammation in the spine as detected by MRI contributes to predicting a BASDAI 50 response in active patients with AS treated with anti-TNF agents.

Ankylosing spondylitis (AS) is a chronic inflammatory disease with a prevalence of between 0.2 and 0.6% in the general population. Until recently treatment options were limited.¹ From this background the strong efficacy of the tumour necrosis factor (TNF) α blockers infliximab,^{2,3} etanercept,^{4,5} and adalimumab,^{6,7} with improvements of the clinical disease activity by at least 40–50% (as measured by Assessments of Spondyloarthritis International Society 40% improvement (ASAS 40) or Bath Ankylosing Spondylitis Disease Activity Index 50% improvement (BASDAI 50), respectively) in 50–60% of patients, implicates a breakthrough in the therapy of active AS.

High treatment costs, but also potentially severe side effects, warrant careful selection of patients with AS who may benefit most from anti-TNF therapy. The ASAS international society for spondyloarthritis, a group of experts in the field

of AS, has published recommendations on which patients should be treated with TNF blockers.⁸ Accordingly, patients with AS who are candidates for TNF blockers should have active disease plus objective evidence of active inflammation, such as elevated C reactive protein (CRP), active (acute) inflammatory lesions as detected by MRI, rapid radiological progression and/or other clinical findings. These recommendations were expert opinion driven rather than data based because solid data on which patients have a poor prognosis and which patients respond best to TNF blocker treatment were lacking.

Recently, we identified predictors of a good clinical response to TNF blockers in active AS⁹ by analysing 99 patients with AS from two placebo controlled trials.^{2,10} Predictors of a good clinical response were (1) shorter disease duration, (2) better functional status (as assessed by the Bath Ankylosing Spondylitis Functional Index (BASFI)) and (3) elevated CRP.⁹ In a subsequent study, patients at a younger age (thus earlier in their disease course) were found to also be more likely to respond to anti-TNF treatment.¹¹

In the present study we analysed in the same group of patients⁹ the predictive capacity of the presence and the extent of active inflammatory lesions in the sacroiliac joints and/or spine, as detected by MRI prior to anti-TNF treatment.

METHODS

Patients

Patients with AS participated in two placebo controlled randomised trials with infliximab (n = 69) and etanercept (n = 30), respectively.^{2,10} MRI was not part of the original study protocols^{2,10} but was performed at selected sites with interest in MRI. Thus, MRI scans at baseline and prior to treatment were only available for 62 out of 99 patients (spine n = 46, SI joints n = 42, spine and SI joints n = 26).

A major clinical response was defined as an improvement of at least 50% of the initial BASDAI (BASDAI 50) after 12 weeks of treatment with either anti-TNF agent. In patients who were treated initially with placebo in these trials, the response to anti-TNF was assessed 12 weeks after switch from placebo to drug (either infliximab or etanercept) during the blinded part of the trial. The BASDAI 50 response was chosen as the outcome parameter since this parameter is easy to calculate and has been suggested to be used in daily practice according to the ASAS recommendations.⁸

Prediction analyses were also performed using ASAS 40 and ASAS 5/6 (percentage of subjects who had at least 20% improvement in 5 of the 6 ASAS domains) response criteria.¹²

Scoring of MR images

Scoring of the spine was performed using a modification of the ankylosing spondylitis spine MRI activity (ASspiMRI a) score¹³ referred to as Berlin MRI spine score,⁶ which has recently been validated in a multi reader exercise.^{14 15} According to the Berlin MRI spine score the extent of bone marrow oedema (irrespective of concomitant erosions) is scored from 0–3 for each vertebral unit (fig 1A). Given 23 vertebral units from C2/C3 to L5/S1, the Berlin score ranges from 0–69.

For the SI joints, the iliac and sacral part of each SI joint were scored from 0–3 (for none, little, moderate or severe inflammation), resulting in a score of between 0 and 12 (fig 1B). This score, referred to as global score for SI joints, has also been recently validated.¹⁶ MRIs in this study were scored by two readers (MR, SS) by consensus. The readers were completely blinded to any clinical data at the time of the scoring.

Statistics

For statistical analysis, the χ^2 test, Student t test and non parametric tests such as the Kruskal Wallis test, Jonckheere Terpstra test and the Mann Whitney U test were performed as appropriate. Correlation coefficients were calculated by means of Spearman rho. Logistic regression analysis was applied to capture factors independently contributing to a major clinical response. All analyses were carried out using SPSS V.13.0 (SPSS Inc., Chicago, Illinois, USA).

RESULTS

Clinical data at baseline

Demographic and clinical parameters of patients who underwent MRI investigation are shown in table 1.

Since MRI was performed in subsets of patients who participated in the two randomised controlled trials (RCTs), we first compared patients with and without MRI. There were no significant differences between patients for whom MRI scans of the spine (n=46) or the SI joints (n=42) were available and patients without MRIs (n=53 and n=57,

respectively) regarding clinical parameters at baseline and response rates that makes selection bias less likely (data not shown).

MRI findings

A positive MRI (defined by a score of at least 1) of either spine or SI joints was found in 49 of 62 patients (79%). MRI findings are shown in table 1. As reported previously,¹⁷ the major site of active inflammation in the spine was the thoracic spine (mean (SD) score 3.8 (4.5)) followed by the lumbar spine (0.9 (1.3)) and the cervical spine (0.5 (1.4)).

MRI inflammation in relation to other parameters of disease activity

At the time of inclusion in the RCTs all patients had active disease with a BASDAI score of at least 4 despite use of non steroidal anti inflammatory drugs (NSAIDs). In this group of active patients, there was no significant correlation between the extent of active inflammatory lesions in the spine (Berlin MRI spine score; n=46) and BASDAI, morning stiffness, global pain, patient global, doctor global, CRP and erythrocyte sedimentation rate (ESR) (Spearman rho correlation coefficients were –0.033, –0.078, 0.016, –0.025, –0.022, 0.136 and 0.195, respectively) nor with the extent of active lesions on MRI in SI joints (n=26, correlation coefficient 0.022). Moreover, there was no correlation between the Berlin MRI spine score (n=46) and BASFI (–0.163) or Bath Ankylosing Spondylitis Metrology Index (BASMI; 0.235).

Similarly, active inflammatory lesions in the SI joints (n=42) did not correlate with parameters of disease activity either: Spearman rho coefficients were 0.001 for BASDAI, 0.158 for morning stiffness, –0.038 for global pain, –0.068 for patient global, –0.134 for doctor global, –0.170 for CRP, –0.070 for ESR and –0.162 for BASFI. However, active inflammatory lesions of the SI joints were negatively correlated with spinal mobility as assessed by BASMI (Spearman rho coefficient –0.499; p=0.001).

MRI inflammation in relation to disease duration

Overall, there was no correlation between the Berlin MRI spine score and disease duration (Spearman rho coefficient –0.180;

Figure 1 A. The Berlin MRI spine score^{14 15} is a modification of the ankylosing spondylitis spine MRI-activity (ASspiMRI-a) scoring system for active inflammatory lesions of the spine. In contrast to the original ASspiMRI-a,¹³ only bone oedema, irrespective of concomitant erosions, is graded from 0 to 3 according to the extent of active inflammation (area of bone oedema). Each vertebral unit from C2/C3 to L5/S1 is scored (23 units). The scoring of active inflammatory lesions (activity score) is shown schematically (modified from Braun *et al*).¹³ B. Scoring system for the sacroiliac (SI) joints.¹⁶ SI joints are divided into halves (ileal part and sacral part) and the extent of active inflammation (bone oedema) is scored as absent (grade 0), little (grade 1), moderate (grade 2), or severe/extended (grade 3). An example of active inflammation and assigned scores is shown.

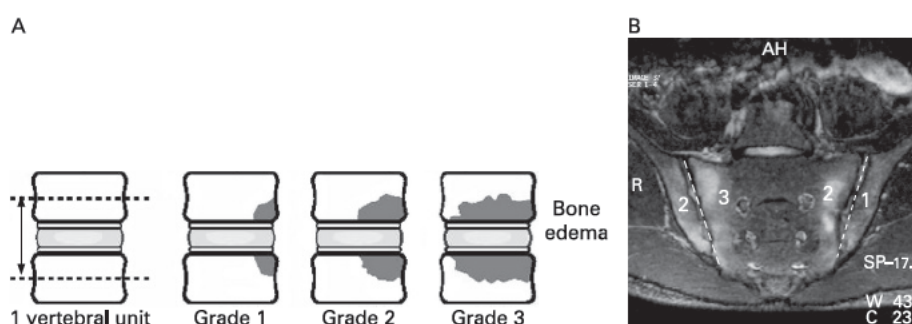


Table 1 Baseline clinical, demographic and MRI characteristics of patients with MRI of the spine, sacroiliac (SI) joints or of both sites

	MRI spine (n = 46)	MRI sacroiliac joints (n = 42)	MRI spine and sacroiliac joints (n = 26)
Demographic and clinical parameters:			
Age (years)*	38.1 (9.0)	37.9 (9.0)	38.1 (9.6)
Disease duration (years)	14.6 (8.8)	14.5 (8.9)	13.9 (9.2)
Male sex (%)	65.2	59.5	57.7
HLA-B27 positive (%)	89.1	87.8	84.6
BASDAI at baseline	6.5 (1.2)	6.5 (1.3)	6.6 (1.4)
BASFI at baseline	5.5 (2.1)	5.1 (2.1)	5.4 (2.2)
BASMI at baseline	3.7 (2.1)	3.6 (2.0)	3.8 (2.0)
CRP at baseline	24.4 (23.7)	23.1 (18.6)	22.5 (17.5)
Patients (%) with:			
CRP >6 mg/litre†	73.9	71.4	73.1
CRP >25 mg/litre	37.0	38.1	38.5
MRI:			
Berlin MRI spine score:			
Total spine (range)	5.2 (6.1) (0–23)	–	4.7 (6.3) (0–23)
Cervical spine (range)	0.5 (1.4) (0–6)	–	0.4 (1.3) (0–6)
Thoracic spine (range)	3.8 (4.5) (0–16)	–	3.5 (4.7) (0–14)
Lumbar spine (range)	0.9 (1.3) (0–4)	–	0.8 (1.2) (0–4)
MRI SI joints score (range)	–	2.3 (2.6) (0–10)	2.2 (2.4) (0–8)
Patients (%) with MRI spine score ≥1	73.9	–	65.4
Patients (%) with MRI SI joint score ≥1	–	61.9	65.4
Clinical response			
ASAS 20 response (%)	73.9	73.8	73.1
ASAS 40 response (%)	56.5	61.9	57.7
ASAS 5/6 response (%)	58.7	66.7	61.5
BASDAI 50 response (%)	54.3	61.9	57.7

In total, MRIs were available from 62 patients. Of these, 46 patients had MRIs of the spine and 42 patients had MRIs of the SI joints; in 26 of the 62 patients MRIs of spine and SI joints were available.

*Mean (SD) values are given if not indicated otherwise. †Normal range for CRP is ≤6 mg/litre.

ASAS, Assessments of Spondyloarthritis; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Spondylitis Functional Index; BASMI, Bath Ankylosing Spondylitis Metrology Index; CRP, C-reactive protein; HLA, human leukocyte antigen.

$p = 0.2$). When patients were grouped according to disease duration, there was a tendency for more active inflammatory lesions being present in the spine in patients with shorter disease duration: the mean (SD) (median) MRI score was 7.4 (6.9) (5.0) in patients with a disease duration of <10 years ($n = 18$), 4.9 (6.6) (2.5) if disease duration was 10–19 years ($n = 12$), and 2.9 (3.7) (1.5) if disease duration was ≥20 years (Kruskal Wallis test $p = 0.14$; Jonckheere Terpstra trend test $p = 0.04$).

With regard to SI joints, however, patients with shorter disease duration had more active inflammation on MRI (Spearman rho coefficient -0.385 ; $p = 0.012$). The mean (SD) (median) of SI joint scores was 3.8 (3.3) (2.5), 1.0 (1.3) (0) and 1.6 (1.9) (0) in patients with disease duration <10 years ($n = 16$), 10–19 years ($n = 12$) and ≥20 years ($n = 14$), respectively (Kruskal Wallis test $p = 0.027$; Jonckheere Terpstra trend test $p = 0.045$). Thus, it seems that more active inflammation is present in the SI joints during the first 10 years of disease as compared to later disease stages, whereas in the spine this relation is less strong.

MRI and response to anti-TNF therapy

Spine

A BASDAI 50 response after 12 weeks of therapy with anti TNF was found in 54.3% (25/46) of patients with MRIs of the spine. A positive MRI of the spine defined by a score of ≥1 did not differentiate between responders (84%) and non responders (62%; $p = 0.1$). Four of 12 patients (33.3%) with a negative MRI

were BASDAI 50 responders. Therefore, a positive MRI (score ≥1) of the spine alone was not predictive of a BASDAI 50 response, and a negative MRI alone did not exclude such a response.

However, when the extent of inflammatory lesions in the spine was considered and related to the BASDAI 50% response rate, the mean (SD) Berlin MRI spine score was higher in BASDAI 50 responders (7.2 (7.2)) compared to non responders (2.9 (3.4); $p = 0.04$). The distribution of the Berlin MRI spine score data among responders and non responders in relation to CRP values is shown in fig 2A. As can be seen from fig 2A, all but one of the patients with high MRI spine scores at baseline were BASDAI 50 responders. Looking at the three spinal segments separately in responders vs non responders, the mean (SD) scores were 0.9 (1.8) vs 0.1 (0.2) ($p = 0.026$) for the cervical spine, 5.2 (5.2) vs 2.1 (2.8) ($p = 0.038$) for the thoracic spine and 1.0 (1.4) vs 0.7 (1.2) ($p = 0.2$) for the lumbar spine, respectively. Thus, responders had more active inflammation in all three spinal segments than non responders.

Univariate logistic regression analyses revealed the Berlin MRI spine score to be a significant predictor of response (odds ratio (OR) = 1.16, 95% CI 1.02 to 1.33; $p = 0.029$). Univariate logistic regression analysis of other parameters revealed only disease duration (OR 0.9, 95% CI 0.83 to 0.97; $p = 0.008$) as a significant predictor but not CRP, BASFI, or BASDAI.

CRP, BASFI, BASDAI and disease duration were then incorporated as potential confounders using multivariate logistic regression analysis. Adjustment for CRP (OR 1.160,

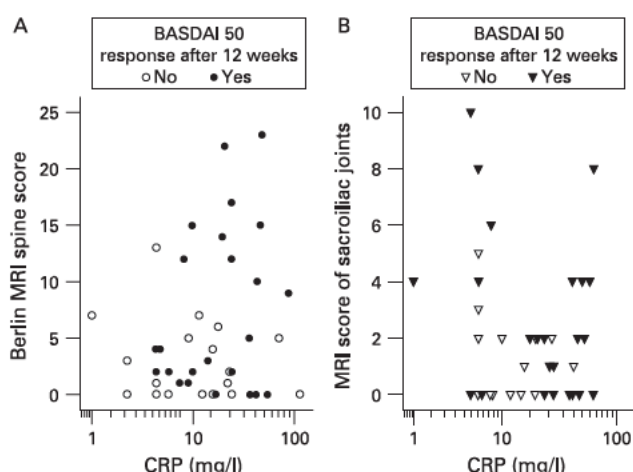


Figure 2 Distribution of baseline MRI scores of the spine (Berlin MRI spine score) in 46 patients (A), and of MRI scores of sacroiliac (SI) joints in 42 patients (B) in relation to classification as Bath Ankylosing Spondylitis Disease Activity Index 50% improvement (BASDAI 50) responders (filled circles or triangles, respectively) or non-responders (open circles or triangles, respectively) after 12 weeks of anti-TNF therapy, and in relation to the respective C-reactive protein (CRP) levels at baseline. As can be seen, patients with high MRI scores of the spine or the SI joints tend to be BASDAI 50 responders. Raw data are shown, CRP levels are depicted on a logarithmic scale.

95% CI 1.011 to 1.331; $p = 0.035$), BASFI (OR 1.162, 95% CI 1.015 to 1.331; $p = 0.030$) and for BASDAI (OR 1.168, 95% CI 1.015 to 1.345; $p = 0.030$) did not alter the predictive capacity of the Berlin MRI spine score. Though adjustment for disease duration, which appeared as the strongest possible confounder, led to loss of statistical significance, the OR for the Berlin MRI spine score was only marginally altered (OR 1.142, 95% CI 0.987 to 1.321; $p = 0.075$). Overall, from this data it appears that the extent of active inflammation on MRI is relevant in predicting the BASDAI 50 response.

SI joints

Among the patients with MRI of SI joints, 61.9% (26/42) were BASDAI 50 responders. Slightly more responders (65%) than non responders (56%) had a MRI SI joint score of ≥ 1 ($p = 0.7$). Similar to the spine, the mean (SD) SI joint score was slightly higher in responders (2.8 (3.0)) as compared to non responders (1.4 (1.6); $p = 0.2$). Figure 2B depicts the distribution of MRI SI joint scores among responders and non responders in relation to CRP. Similar to the spine, most of the patients with high SI joint scores at baseline were responders. Univariate logistic regression analysis, however, revealed a trend only for MRI SI score (OR = 1.28, 95% CI 0.94 to 1.74; $p = 0.076$). Thus, in this group of patients with longstanding AS MRI of SI joints did not predict a BASDAI 50 response.

Spine and SI joints

MRI scans of the SI joints and the spine were available for 26 patients (table 1). Of these 26 patients, 11 (42.3%) showed active inflammation at both sites (spine and SI joints) and 7 of these (63.6%) were BASDAI 50 responders. Interestingly, 6 of 26 (23.1%) had active inflammatory lesions in the spine but not in the SI joints (4 of these 6 patients (66.7%) were BASDAI 50 responders), and 6 of 26 (23.1%) also had active inflammation in the SI joints but not in the spine (4 patients (66.7%) were

BASDAI 50 responders). Only 3 (11.5%) of the 26 patients had no active inflammation at either site, none of these 3 patients achieved BASDAI 50 response.

BASFI and CRP and response to anti-TNF therapy

In line with our previous study,⁹ there was a trend for a lower BASFI (mean (SD) 5.0 (2.1) vs 6.0 (2.0); $p = 0.10$) and higher CRP values (mean (SD) 27.9 (21.2) mg/litre vs 20.2 (26.2) mg/litre; median 24.0 mg/litre vs 12.0 mg/litre; $p = 0.034$) in responders as compared to non responders in patients ($n = 46$) with MRI of the spine (see also fig 2). Moreover, the proportion of patients with an elevated CRP was higher among responders compared to non responders (CRP > 6 mg/litre: 88% vs 57%, $p = 0.023$ and CRP ≥ 10 mg/litre: 64.5% vs 35%, $p = 0.047$, respectively).

ASAS 40 and ASAS 5/6 as outcome criteria

The comparison between responders and non responders and analysis of predictors were almost identical when ASAS 40 instead of BASDAI 50 was applied as outcome criterion for a good clinical response, and very similar when ASAS 5/6 was used (data not shown).

Prediction of BASDAI 50 response in clinical practice

Based on our data we tried to assign predictive values for CRP, MRI and disease duration by calculating likelihood ratios (LR) for various ranges of values of these parameters. As can be seen in table 2, only short disease duration (< 10 years), high Berlin MRI spine scores (≥ 11) and high CRP levels (≥ 40 mg/litre) provided predictive information whereas intermediate values were not informative.

While each parameter on its own had moderate predictive capacity at most, the three predictive parameters in combination were quite predictive: a patient with a disease duration of ≥ 20 years (LR 0.28), a normal CRP (LR 0.28) and a normal MRI of the spine without signs of active inflammation (LR 0.42), for example, has an LR product of 0.033 ($0.28 \times 0.28 \times 0.42 = 0.033$).

Table 2 Likelihood ratios (LR) for disease duration, C-reactive protein (CRP) levels and Berlin MRI score in predicting a Bath Ankylosing Spondylitis Disease Activity Index 50% improvement (BASDAI 50) response in patients with active ankylosing spondylitis (AS)

Parameter	Patients (n) with BASDAI 50 response	Patients (n) without BASDAI 50 response	LR*
Disease duration:			
≥ 20 years	4	12	0.28
10–19 years	6	6	0.84
< 10 years	15	3	4.20
CRP (mg/litre):			
< 6	3	9	0.28
6–24.9	10	7	1.20
25–39.9	4	3	1.12
≥ 40	8	2	3.37
Berlin MRI spine score:			
0	4	8	0.42
1–4	10	7	1.43
5–10	3	5	0.50
≥ 11	8	1	6.67
Total†	25	21	

*LR = likelihood ratio, defined as sensitivity/(100-specificity). †The total population ($n = 46$) comprises patients with AS for whom MRI of the spine prior to anti-TNF treatment was available.
TNF, tumour necrosis factor.

and a post test probability of achieving BASDAI 50 of only 3.7%. Thus, such a patient is prone to be a non responder. By contrast, a patient with a disease duration of <10 years (LR 4.2), a CRP of ≥ 40 mg/litre (LR 3.37) and an MRI spine score of ≥ 11 (LR 6.67) has an LR product of 113.17 ($4.2 \times 3.37 \times 6.67 = 113.17$), a probability to achieve a BASDAI 50 response of 99.1% and, therefore, is prone to be a BASDAI 50 responder (for calculation of the post test probability from LR product see Sackett *et al*¹⁸ or Rudwaleit *et al*¹⁹ (appendix)).

The presence of one or more of the three predictive parameters (disease duration <10 years, CRP ≥ 40 mg/litre, Berlin MRI spine score ≥ 11) was significantly associated with BASDAI 50 improvement ($\chi^2 = 12.4$; $p = 0.004$). As can be seen from fig 3, all patients with two or three predictive parameters representing 26% of the total population achieved BASDAI improvements of at least 45%. Among the patients who were positive for just one of the three predictive parameters, all but one patients improved by at least 25%. A probability model taking into account disease duration, CRP (using a cut off value of 10 mg/litre) and Berlin MRI spine score based on our data is shown in fig 4. Figure 4 illustrates that each variable might be of additional value in the prediction of a good clinical response.

DISCUSSION

TNF blocking agents have become a major class of drugs in the treatment of active AS. High treatment costs, however, warrant careful selection of patients who are likely to benefit most. We have shown previously that shorter disease duration, better functional status and elevated CRP levels correlate with a BASDAI 50 response.⁹ Here, we show that active inflammation

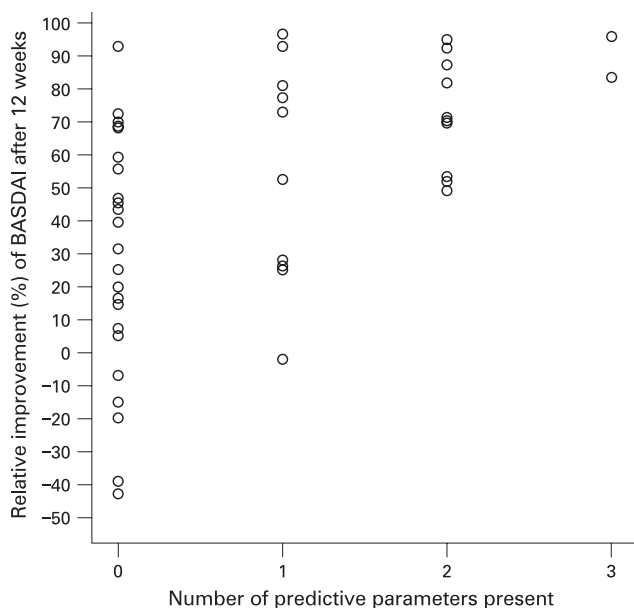


Figure 3 Relative improvement (%) of the initial Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) in individual patients after 12 weeks of anti-tumour necrosis factor (TNF) therapy in relation to the presence of none, one, two or three of three predictive parameters. The three parameters were (1) disease duration <10 years; (2) C-reactive protein (CRP) ≥ 40 mg/litre; and (3) Berlin MRI spine score ≥ 11 . As can be seen, all patients with two or more parameters had a BASDAI improvement of at least 45%, and all but one patient with one parameter had a BASDAI improvement of at least 25%.

in the spine by MRI appears to have an additional predictive value. While the presence of only few and small active inflammatory lesions on MRI did not have any discriminative capacity, more extended active inflammation in the spine was significantly associated with a good clinical response. Because the sample size of this study ($n = 46$) was relatively small, we are aware that larger sample size studies may give slightly different figures.

The predictive capacity of the Berlin MRI spine score, disease duration and CRP was moderate at most when considered solely. However, when we combined the three parameters (Berlin MRI spine score, CRP and disease duration) the prediction model clearly improved. Patients with short disease duration, high CRP and high MRI scores were prone to be responders (probability of 99%). All patients with at least two of these three predictive parameters representing 26% of the total population achieved a BASDAI improvement of at least 45%. All but one of the patients with at least one of these three predictive parameters improved by at least 25%. By contrast, patients with long disease duration, normal CRP and no active inflammatory lesion in the spine on MRI were highly unlikely to achieve BASDAI 50 response (probability to be a non responder of 96.3%).

In patients with AS with a BASDAI ≥ 4 it can be sometimes difficult for the clinician to decide whether the patient's pain and symptoms are attributable to active inflammation or rather related to mechanical conditions, such as degenerative changes including eg, herniated discs. The BASDAI score by itself does not differentiate between various causes of back pain. The lesson to be learnt from this study is that anti TNF agents work best if there is strong and cumulative evidence of substantial active inflammation. Such evidence can be obtained from CRP measurement and MRI studies, and can be inferred from disease duration in that the shorter the disease duration, the more likely the presence of an underlying active inflammation is the cause for a high BASDAI.

The patients studied herein had rather longstanding AS (mean disease duration 14 years). At least one active inflammatory lesion in the spine was present in 73.9% of patients, a figure very similar to the 77.4% reported from the Ankylosing Spondylitis Study for the Evaluation of Recombinant Infliximab Therapy (ASSERT) trial.²⁰ Since spinal inflammation may predominate in active longstanding AS, it may come as no surprise to find that the predictive value of MRI of the spine was better than that of the SI joints. However, this finding should not generally preclude a predictive role of MRI of SI joints in patients with earlier disease; a population that warrants further study. Of note, almost a quarter (23%) of the patients in our study for whom MRI of spine and SI joints were available had active inflammation in the SI joints, but not in the spine. Accordingly, MRI studies of the spine without SI joints may not suffice to comprehensively assess active axial inflammation in AS.

It is known that CRP and ESR correlate poorly with clinical disease activity in AS.²¹ In our study, MRI scores of the spine did not correlate at all with other disease activity markers including BASDAI, patient global, morning stiffness, CRP and ESR. To our knowledge, no other study has tempted to correlate MRI inflammation of the spine with disease activity markers. In the original description of the ASSpiMRI,¹² as in another report²² (both on 20 patients), only data on correlation of MRI change scores with clinical change scores upon anti TNF therapy were presented, not data on status scores for MRI and clinical disease

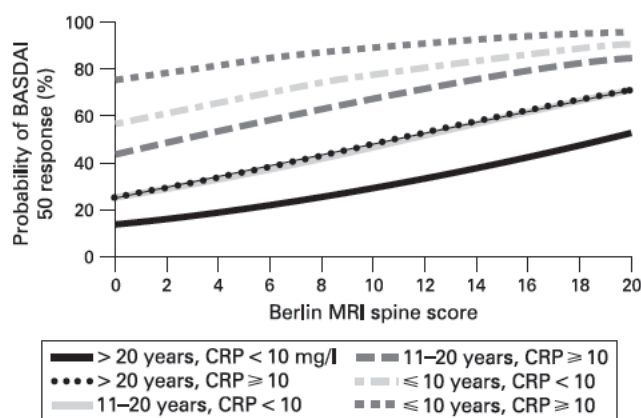


Figure 4 Probability curves (model) of achieving a Bath Ankylosing Spondylitis Disease Activity Index 50% improvement (BASDAI 50) response according to Berlin MRI spine score (x-axis) and different categories of disease duration (≤ 10 years, 11–20 years, >20 years) and of C-reactive protein (CRP) levels (<10 mg/litre vs ≥ 10 mg/litre), respectively.

activity parameters. Similarly, in the ASSERT MRI study no correlation with status scores was performed.²⁰

Similar to the spine, active inflammation of the SI joints on MRI did not correlate with disease activity. An earlier study on 41 patients from Denmark also did not find a correlation of MRI of SI joints with CRP,²³ and a study on 19 patients from Korea²⁴ and a study on 18 patients from the US had similar results.²⁵ Of note, however, was the finding in the study from Denmark,²³ as in our study, that more extensive active inflammation of SI joints was found in patients with a shorter disease duration. Thus, active inflammation of SI joints may predominate during early stages of AS, whereas such a relationship is less clear for the spine.

To summarise, a short disease duration, high CRP levels and widespread spinal inflammation on MRI all contribute to predict a BASDAI 50 response in patients with active AS after 12 weeks of treatment with TNF blockers. Patients with two or three of these parameters are highly likely to achieve a good response. By contrast, the combination of long disease duration, normal values for CRP and no active inflammatory lesions on MRI is highly predictive of not being a BASDAI 50 responder.

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