

Original article

The Ankylosing Spondylitis Disease Activity Score is a highly discriminatory measure of disease activity and efficacy following tumour necrosis factor- α inhibitor therapies in ankylosing spondylitis and undifferentiated spondyloarthropathies in China

Manlong Xu^{1,*}, Zhiming Lin^{1,*}, Xinghe Deng², Li Li¹, Yanlin Wei¹, Zetao Liao¹, Qiuxia Li¹, Qiuqing Wei¹, Zaiying Hu¹, Yanli Zhang¹, Qu Lin¹, Jianlin Huang¹, Tianwang Li¹, Yunfeng Pan¹, Yuqiong Wu¹, Ou Jin¹, Buyun Yu¹ and Jieruo Gu¹

Abstract

Objective. To validate the clinical value of the new Ankylosing Spondylitis Disease Activity Scores (ASDASs) in assessing the disease activity and efficacy of TNF- α inhibitor in AS and uSpA patients in China.

Methods. Two hundred and thirty patients were included in our study. They consisted of patients with active AS ($n=87$) and uSpA ($n=30$) participating in a double-blind placebo-controlled randomized clinical trial of etanercept and patients with active AS ($n=58$) and uSpA ($n=55$) treated with infliximab. The disease activity and treatment effects were assessed by ASDAS, BASDAI, patient global and the acute inflammation score of lumbar and SI joints by MRI. Discriminatory ability of all the measures was analysed by standardized mean difference and t -score.

Results. In both the AS and uSpA groups, ASDAS correlated well with patient global score (AS group: $r=0.65$ – 0.72 ; uSpA group: $r=0.52$ – 0.62), ESR (AS group: $r=0.57$ – 0.81 ; uSpA group: $r=0.63$ – 0.85) and CRP (AS group: $r=0.51$ – 0.70 ; uSpA group: $r=0.61$ – 0.76) both at baseline and in changes from baseline to 6 weeks after TNF- α inhibitor treatment. The ASDAS scores outperformed BASDAI, patient global score, ESR, CRP and the acute inflammation score by MRI in differentiating patients with different levels of disease activity and patients with different levels of change in both AS and uSpA groups. There was little difference in performance between the two versions of the ASDAS.

Conclusion. The new ASDAS is a highly effective measure in assessing disease activity and a great discriminatory measurement to assess the efficacy of TNF- α inhibitor in Chinese AS patients and uSpA patients.

Key words: Ankylosing spondylitis, Undifferentiated spondyloarthropathy, Ankylosing spondylitis disease activity scores, Magnetic resonance imaging, Tumour necrosis factor- α inhibitor.

¹Department of Rheumatology and ²Department of Radiology, The Third Affiliated Hospital of Sun Yat-Sen University, Guangzhou, China. Submitted 14 April 2010; revised version accepted 26 January 2011.

Correspondence to: Jieruo Gu, Department of Rheumatology, The Third Affiliated Hospital of Sun Yat-Sen University, 600 Tianhe Road, Guangzhou 510630, China. E-mail: gujieruo@163.com

*Manlong Xu and Zhiming Lin contributed equally to this work.

Introduction

AS is a chronic inflammatory disorder of the spine and entheses, which also affects skeletal and extra-skeletal tissues. AS occurs particularly in young men in the workforce and leads to a significant health burden to the community [1]. uSpA is one of the commonest subtypes of SpA. The estimated prevalence is 0.67% [2], and >50%

of these patients will develop AS within 5–10 years [3]. The activity of AS reflects the level of inflammation, predicts prognosis and influences treatment decisions. Currently, the most accepted and widely used measure for assessing the disease activity of AS and uSpA is the BASDAI [4]. However, BASDAI is a self-administered patient-directed questionnaire and does not include any objective measures of activity. It cannot reflect the whole spectrum of disease activity of AS or uSpA. In addition, MRI is also used to assess the disease activity of SpA. The current recommendations of the Assessment of SpondyloArthritis International Society (ASAS) proposed MRI as one of the two primary assessments for the classification of AS, with identification of bone marrow oedema (osteitis) in the SI joint [5]. Indeed, in early studies, the acute inflammation score of lumbar MRI correlated well with BASDAI ($r=0.6$, $P=0.005$) and current studies are distinguishing MRI changes in the cartilaginous and the ligamentous portions of the SI joint [6–10]. However, because the practicability and expense of serial MRI limits its use in a worldwide arena, we need to validate a comprehensive, practical and sensitive measurement to assess the disease activity and efficacy of different therapies in AS and other uSpA.

Recently, the ASAS developed four new candidate indices for assessing disease activity in AS called the Ankylosing Spondylitis Disease Activity Score (ASDAS) (see supplementary table 1, available as supplementary data at *Rheumatology* Online) [11]. They were primarily applied in the white and black race and showed good clinical value [11, 12]. Based on feasibility issues, the ASAS selected the ASDAS consisting of total back pain, duration of morning stiffness, the BASDAI question on peripheral joints, patient global score of disease activity and CRP as the preferred ASDAS (ASDAS with CRP). As an alternative the ASDAS with ESR, which consists of the same variables apart from the acute-phase reactant, can be used if CRP is not available. However, there was no validation in China. Therefore, we sought to validate the two versions of the ASDAS in AS and uSpA patients responding to TNF- α inhibitors in China.

Methods

Patients

Two hundred and thirty patients treated with TNF- α inhibitor were recruited from the Third Affiliated Hospital of Sun Yat-Sen University in Guangzhou, China. They consisted of two cohorts: (i) 117 patients with active disease (including 87 patients with AS and 30 patients with uSpA) participated in a 12-week double-blind placebo-controlled randomized clinical trial with etanercept (43 patients with AS and 15 patients with uSpA) and placebo (44 patients with AS and 15 patients with uSpA). The initial etanercept or placebo treatments continued for 6 weeks, and each group received etanercept from 6 to 12 weeks). Thus, patients in the TNF- α group received etanercept 50 mg weekly for 12 weeks. (ii) A total of 113 patients with active disease (including 58 patients with AS and 55

patients with uSpA) were treated with infliximab, 5 mg/kg, at Weeks 0, 2, 6 and 12. During the study, only NSAIDs and/or SSZ were permitted in a stable dose for at least 3 months before the treatment with TNF- α inhibitors. The inclusion criteria for disease activity at baseline included: (i) BASDAI ≥ 4 and/or (ii) patient global score ≥ 4 (all scores on a scale of 0–10) or an elevated ESR (>20 mm/h) or an elevated CRP (>6 mg/l). All the AS patients fulfilled the modified New York criteria [13], and all the uSpA patients fulfilled the ESSG criteria, but not any criteria for the current established diseases in this group (such as AS, ReA, PsA and IBD-associated arthritis) [14]. In addition, all the uSpA patients included in the study described a back pain and fulfilled the ASAS classification criteria for axial SpA [5]. This study was approved by the Clinical Ethics Review Board of the Third Affiliated Hospital of Sun Yat-Sen University, and the subjects' written consent was obtained according to the Declaration of Helsinki at their admission.

Data collecting

All the following data for disease activity at both baseline and Week 6 of all the patients as well as MRI results of some patients at Week 12 were collected: patient assessment of global disease activity [15], ESR (mm/h), CRP (mg/l), the six individual questions of the BASDAI and the results of lumbar and SI joint MRI (if available). With the data above, the two ASDAS versions and the BASDAI could be calculated. Furthermore, we used the MRI score for acute spinal changes in AS, ASspiMRI-a, to score the acute inflammation of lumbar spine, and MRI score for acute inflammation of the SI joint in AS, developed by Hermann *et al.*, to score the acute inflammation of SI joint [6, 7].

Validation method

We used the following method to investigate the discriminatory capacity of the various disease activity measures.

- (i) Correlation: (a) analyse the correlation between all the measures and patient global score and ESR as well as CRP at baseline; and (b) analyse the correlation between the changes of all the measures and the changes of patient global score, ESR and CRP from baseline to Week 6.
- (ii) Discrimination: (a) analyse the discriminatory capacity of the measures in discriminating different levels of change of disease activity after different treatments; (b) group the patients into high and low disease activity according to patient global score (≥ 4 vs <4), ESR (elevated: >20 mm/h vs normal: ≤ 20 mm/h) and CRP (elevated: >6 mg/l vs normal ≤ 6 mg/l) at baseline, and then analyse the discriminatory capacity of the measures in discriminating disease activity status in different settings; and (c) divide patients into subgroups according to ESR at baseline (elevated vs normal) and peripheral arthritis at baseline (presence vs absence), and then analyse the discriminatory capacity of the measures in different subgroups.

- (iii) MRI measures of inflammation. For the patients who underwent MRI, we add the acute inflammation scores of MRI and do the following analysis: (a) analyse the correlation between MRI scores and the other indices at baseline; and (b) analyse the discriminatory ability of MRI scores, ASDAS and BASDAI in differentiating various levels of disease activity.
- (iv) The two versions of ASDAS were defined as: ASDAS with CRP = $0.121 \times \text{back pain (BASDAI Q2)} + 0.058 \times \text{duration morning stiffness (BASDAI Q6)} + 0.110 \times \text{patient global score} + 0.073 \times \text{peripheral pain/swelling (BASDAI Q3)} + 0.579 \times \text{Ln (CRP + 1)}$; ASDAS with ESR = $0.079 \times \text{back pain} + 0.069 \times \text{duration morning stiffness} + 0.113 \times \text{patient global score} + 0.086 \times \text{peripheral pain/swelling} + 0.293 \times \sqrt{\text{ESR}}$.

Statistical method

All the data were analysed by Pearson's correlation, two-sided, independent-sample *t*-test and linear regression. Discrimination between patients in low vs high disease activity according to various definitions, and between various levels of change was analysed as standardized mean difference (SMD: difference of the group means divided by the pooled s.d. of the group means). The higher the SMD value, the greater the discriminatory is [12, 16]. All statistics were performed by SPSS 11.5 software. A power of 80% and a two-sided significance level of 0.05 were used in the calculation of the difference of disease activity assessed by ASDAS between W_0 and W_{12} . A sample size of 145 was used in the AS group, and 85 subjects were recruited in the uSpA group.

Results

Two hundred and thirty patients, consisting of 145 AS and 85 uSpA were included. Of the AS group, 131 (90%) were male, 125 (86%) were HLA-B27 positive, the mean age was 27.3 (8.0) years, the disease duration was 7.2 (4.8) years and 20 (14%) had positive family history of AS. At baseline, the prevalence of peripheral arthritis in AS group was 56%, the value of CRP was 30.85 (26.11) mg/l and the value of ESR was 20.18 (26.46) mm/h. In the uSpA group, 76 (89%) were male, 53 (62%) were HLA-B27 positive, the mean age was 23.6 (9.9) years, the disease duration was 3.9 (3.9) years and 10 (12%) had positive family history of AS or SpA. At baseline, the prevalence of peripheral arthritis in the uSpA group was 41%, the value of CRP was 29.84 (30.26) mg/l and the value of ESR was 33.50 (25.86) mm/h.

Correlation between all the measures and patient global score as well as ESR and CRP

We analysed the correlation between the measures and patient global score, ESR and CRP at baseline and in the changes after 6 weeks treatment of TNF- α inhibitors (including TNF- α inhibitor groups from 0 to 6 weeks and placebo treatment group from 6 to 12 weeks). The results showed that in the AS group, the two ASDASs correlated well with patient global score (*r* ranged from 0.65 to 0.72), ESR (*r* ranged from 0.57 to 0.81) and CRP (*r* ranged from 0.51 to 0.70) both at baseline and in the changes following therapy. BASDAI correlated well with patient global score (*r* = 0.72 at baseline and 0.66 in the change), but poorly with ESR (0.35 and 0.36) and CRP (0.25 and 0.37). In addition, patient global score correlated poorly with both ESR and CRP. In the uSpA patient group, similar correlations to those that occurred with AS were noted (Table 1).

TABLE 1 Pearson's correlation between the indices at baseline and the changes after 6 weeks treatment with TNF inhibitors

Index	Baseline						Changes					
	PG		ESR		CRP		PG		ESR		CRP	
	<i>R</i>	<i>P</i> -value	<i>R</i>	<i>P</i> -value	<i>R</i>	<i>P</i> -value	<i>R</i>	<i>P</i> -value	<i>R</i>	<i>P</i> -value	<i>R</i>	<i>P</i> -value
AS group (<i>n</i> = 145)												
ASDAS with CRP	0.69	<0.001	0.57	<0.001	0.68	<0.001	0.72	<0.001	0.58	<0.001	0.70	<0.001
ASDAS with ESR	0.65	<0.001	0.81	<0.001	0.51	<0.001	0.72	<0.001	0.77	<0.001	0.57	<0.001
BASDAI	0.72	<0.001	0.35	<0.001	0.25	0.010	0.66	<0.001	0.36	0.001	0.37	<0.001
PG			0.23	0.005	0.27	0.006			0.30	<0.001	0.39	<0.001
ESR, mm/h	0.23	0.005			0.54	<0.001	0.30	<0.001			0.59	<0.001
CRP, mg/l	0.27	0.006	0.54	<0.001			0.39	<0.001	0.59	<0.001		
uSpA group (<i>n</i> = 85)												
ASDAS with CRP	0.52	<0.001	0.68	<0.001	0.76	<0.001	0.62	<0.001	0.63	<0.001	0.66	<0.001
ASDAS with ESR	0.53	<0.001	0.85	<0.001	0.69	<0.001	0.62	<0.001	0.82	<0.001	0.61	<0.001
BASDAI	0.48	<0.001	0.15	0.176	0.20	0.040	0.53	<0.001	0.28	0.009	0.22	0.039
PG			0.17	0.119	0.22	0.042			0.30	0.006	0.27	0.011
ESR, mm/h	0.17	0.119			0.80	<0.001	0.30	0.006			0.78	<0.001
CRP, mg/l	0.22	0.042	0.80	<0.001			0.27	0.011	0.78	<0.001		

PG: patient global score.

TABLE 2 Discrimination between various levels of changes from baseline to Week 6 after different treatments in AS and uSpA groups

Index	TNF inhibitors, mean (s.d.)	Placebo, mean (s.d.)	Standard mean diff (95% CI)	t	P-value
AS group					
Number of cases	101	44			
ASDAS with CRP	2.05 (1.07)	0.53 (0.88)	1.24 (0.95, 1.53)	7.95	<0.001
ASDAS with ESR	1.66 (1.09)	0.56 (0.75)	0.98 (0.66, 1.30)	6.40	<0.001
BASDAI	2.38 (1.92)	1.03 (1.70)	0.67 (0.34, 1.00)	3.85	<0.001
PG	3.16 (2.56)	1.23 (1.73)	0.76 (0.43, 1.09)	5.20	<0.001
ESR, mm/h	21.69 (28.45)	9.27 (20.08)	0.52 (0.13, 0.91)	2.50	0.007
CRP, mg/l	20.80 (26.12)	4.26 (23.94)	0.60 (0.27, 0.93)	3.42	<0.001
uSpA group					
Number of cases	70	15			
ASDAS with CRP	1.86 (1.07)	0.63 (0.78)	1.10 (0.59, 1.61)	5.17	<0.001
ASDAS with ESR	2.22 (1.06)	0.54 (0.58)	1.42 (0.95, 1.89)	8.55	<0.001
BASDAI	2.48 (1.50)	1.21 (1.32)	0.94 (0.33, 1.55)	5.42	<0.001
PG	3.73 (1.84)	1.70 (1.05)	1.07 (0.56, 1.58)	5.83	<0.001
ESR, mm/h	28.12 (29.62)	2.47 (12.97)	0.88 (0.35, 1.41)	5.27	<0.001
CRP, mg/l	20.88 (31.23)	3.30 (8.71)	0.60 (0.05, 1.15)	4.04	<0.001

PG: patient global score.

Discriminatory capacity of the measures

Table 2 presents the discriminatory ability of the measures in differentiating various levels of change (from baseline to Week 6) after TNF- α inhibitor treatment in AS and uSpA groups. The efficacy of treatment in the TNF- α group was assumed to be better than that in the placebo group. It shows that: in the AS group, the ASDAS discriminated best, followed by patient global score, BASDAI, CRP and ESR. Likewise, the two ASDAS versions outperformed the other measurements in differentiating various levels of change in the uSpA group.

In differentiating disease activity status at baseline, the results were as follows. In the AS group, based on the patient global score, the discriminatory power of the two ASDASs were similar to that of BASDAI, but much better than ESR and CRP. In the setting of ESR and CRP based, the two ASDASs outperformed the other assessments (see supplementary table 2, available as supplementary data at *Rheumatology* Online). In the uSpA group, the two ASDAS versions outperformed the other measurements in all settings (see supplementary table 3, available as supplementary data at *Rheumatology* Online).

As we wanted to know whether the various disease activity measures perform equally well in different subgroups, patient were divided into subgroups according to ESR at baseline (elevated vs normal) and peripheral arthritis at baseline (presence vs absence). We investigated the discriminatory ability of the measures again. The results of the AS group showed that the ASDAS scores had good discriminatory power and outperformed the other measures in all four subgroups (see supplementary table 4, available as supplementary data at *Rheumatology* Online). However, the numbers of patients in the subgroups of uSpA were too small and the results

were not statistically significant, so we did not show them here.

Correlation between acute inflammation score of MRI and the other measures and their discriminatory capacity in differentiating disease activity status

In our study, some patients underwent MRI of the lumbar spines and/or SI joint at baseline and/or Week 12. The number of cases was as follows: in the AS group: 44 lumbar and 52 SI joints at baseline and 22 lumbar and 34 SI joints at Week 12; in the uSpA group: 54 lumbar and 56 SI joints at baseline and 43 lumbar and 44 SI joints at Week 12.

Pearson's correlations between the acute inflammation score of MRI and the other measures at baseline in the AS and uSpA groups are shown in Table 3. Obviously, the ASDAS versions outperformed the two MRI scores in correlating with patient global score, ESR and CRP at baseline in both the groups. The acute inflammation score of lumbar MRI performed better in the AS group but worse in uSpA group than SI joint MRI in correlating with the other measures.

Table 4 presents the discriminatory capacity of MRI score, ASDAS, BASDAI, patient global score, ESR and CRP in differentiating disease activity status between baseline and Week 12. It shows that all the scores of the measures declined obviously from baseline to Week 12 after treatment with TNF- α inhibitor. The discriminatory capacity of ASDAS was the best, followed by BASDAI and patient global score, then ESR and CRP. The powers of these results were all >0.990. However, the discriminatory capacity of MRI score seemed to be poor, and had relatively low power. Obviously, in both the AS and uSpA groups, the ASDAS scores performed better than MRI

TABLE 3 Pearson correlations between the acute inflammation score of MRI and the other indices at baseline in AS and uSpA groups

Index	PG		ESR		CRP		L-MRI		SI joint MRI	
	R	P-value	R	P-value	R	P-value	R	P-value	R	P-value
AS group										
Number of cases	75		75		75		44		52	
ASDAS with CRP	0.64	<0.001	0.52	<0.001	0.73	<0.001	0.22	0.147	-0.06	0.673
ASDAS with ESR	0.67	<0.001	0.78	<0.001	0.41	<0.001	0.39	0.010	0.09	0.518
BASDAI	0.66	<0.001	0.32	0.005	0.17	0.152	0.25	0.104	-0.00	0.995
L-MRI	0.11	0.471	0.49	0.001	0.18	0.239			0.25	0.273
SI joint MRI	0.01	0.973	0.16	0.268	-0.16	0.271	0.25	0.273		
uSpA group										
Number of cases	57		57		57		54		56	
ASDAS with CRP	0.64	<0.001	0.74	<0.001	0.80	<0.001	0.21	0.129	0.34	0.010
ASDAS with ESR	0.60	<0.001	0.90	<0.001	0.74	<0.001	0.10	0.480	0.27	0.045
BASDAI	0.45	<0.001	0.32	0.015	0.27	0.040	-0.08	0.559	-0.06	0.681
L-MRI	0.23	0.098	0.07	0.622	0.13	0.364			0.12	0.392
SI joint MRI	0.21	0.123	0.32	0.016	0.38	0.004	0.12	0.392		

L-MRI: lumbar MRI; PG: patient global score.

TABLE 4 Discriminatory ability of the acute inflammation score of MRI, ASDAS, BASDAI, patient global score, ESR and CRP in differentiating various levels of disease activity between baseline and Week 12

Index	W ₀ , mean (s.d.)	W ₁₂ , mean (s.d.)	Standard mean difference (95% CI)	t	P-value
AS group					
Number of cases	75	39			
ASDAS with CRP	3.12 (0.99)	1.22 (0.83)	1.46 (1.18, 1.74)	10.24	<0.001
ASDAS with ESR	3.04 (0.95)	1.30 (0.75)	1.44 (1.16, 1.72)	9.94	<0.001
BASDAI	4.25 (1.54)	1.59 (1.57)	1.33 (1.03, 1.63)	8.69	<0.001
L-MRI	6.11 (6.03) (n=44)	3.02 (3.06) (n=22)	0.57 (0.07, 1.07)	2.77	0.007
SI joint MRI	8.14 (5.63) (n=52)	6.54 (3.95) (n=34)	0.32 (-0.12, 0.76)	1.45	0.152
PG	5.28 (2.13)	1.90 (1.99)	1.28 (0.97, 1.59)	8.20	<0.001
ESR	30.60 (22.26)	9.03 (8.00)	1.26 (0.84, 1.68)	7.47	<0.001
CRP	19.76 (18.47)	4.07 (5.45)	0.92 (0.57, 1.27)	6.78	<0.001
uSpA group					
Number of cases	57	44			
ASDAS with CRP	3.21 (1.02)	0.78 (0.72)	1.61 (1.37, 1.85)	13.75	<0.001
ASDAS with ESR	3.10 (0.97)	0.81 (0.56)	1.63 (1.40, 1.86)	14.64	<0.001
BASDAI	4.56 (1.00)	0.90 (0.70)	1.47 (1.33, 1.61)	11.15	<0.001
L-MRI	0.54 (1.35) (n=54)	0.28 (1.03) (n=43)	0.21 (-0.18, 0.60)	1.03	0.304
SI joint MRI	7.32 (3.61) (n=56)	4.80 (3.44) (n=44)	0.66 (0.29, 1.03)	3.54	0.001
PG	4.75 (1.95)	0.88 (0.83)	1.54 (1.30, 1.78)	14.70	<0.001
ESR	34.97 (28.87)	7.84 (15.48)	0.98 (0.64, 1.32)	5.91	<0.001
CRP	30.20 (33.53)	6.21 (17.36)	0.79 (0.43, 1.15)	4.56	<0.001

L-MRI: lumbar MRI; PG: patient global score.

score. In the AS group, the discriminatory power of the acute inflammation score of lumbar MRI was stronger than SI joint MRI, whereas in the uSpA group the acute inflammation score of SI joint MRI outperformed lumbar MRI in most settings.

Discussion

There is much variety in the clinical picture among different patients with AS. Likewise, patients with uSpA have atypical clinical manifestations and uncertain

development and prognosis. Therefore, it is especially difficult to evaluate disease activity in both kinds of disease. Nowadays, there is still no precise, convenient and special measurement for assessing the disease activity and efficacy of treatment in AS, and we also lack a suitable disease activity measurement for uSpA. After the development of the new ASDAS, there were two initial studies showing that the ASDAS was of highly discriminatory power in assessing disease activity in AS [11, 12]. Our study shared the same point of view as the two studies. There is no previous report about the ASDAS in a Chinese population. Our study is the first to show that the ASDAS can be used in assessing the disease activity in AS and uSpA patients in China.

AS patients rate disease activity on the basis of complaints, whereas physicians rate disease activity on the basis of instruments related to disease severity and inflammation [17]. The correlation between the assessment of the two perspectives is poor ($r=0.30$) and they do not necessarily reflect the same construct [12]. It is necessary to include both the perspectives in an index. However, the former indices either assess disease activity from the patient perspective or from the physician perspective [17, 18]. Therefore, they cannot represent the whole disease activity. Differently, the ASDAS scores were developed to include both patient-reporting assessment and acute-phase reactant and have high face validity. The studies of Lukas *et al.* [11] and van der Heijde *et al.* [12] showed that the ASDAS correlated well with both doctor and patient perceptions of disease activity. Similarly, in our study, we used the ASDAS in both AS and uSpA patients in China. It showed that, in both AS and uSpA patients, the two ASDAS versions correlated well with both patient-reported assessment (patient global score) and acute-phase reactants (ESR and CRP), and had strong discriminatory power in differentiating patients with various levels of disease activity and with different levels of change. The performance of ASDAS was the best in comparison with BASDAI, patient global score, ESR, CRP and the acute inflammation score of MRI. Furthermore, another study showed that ASDAS also demonstrated construct validity and high responsiveness during treatment with TNF- α inhibitors in SpA patients [19]. According to all the studies mentioned above, we may come to a conclusion that, in comparison with all the former measures, in assessing the disease activity of SpA patients, the ASDAS can represent the whole disease activity better and have a stronger discriminatory power, showing a higher clinical value. The high discriminatory capacity of the ASDAS can be used in differentiating disease activity status and is very important in the assessment of treatment efficacy in clinical trials.

Our study showed that the ASDAS outperformed the other disease activity measures with respect to discriminatory ability in all the subgroups with elevated or normal baseline ESR and with presence or absence of peripheral arthritis at baseline. The same results were also shown in the study of van der Heijde *et al.* [12]. In that study, they

also tested whether there was a possible influence of gender. The result showed that the ASDAS performed best with respect to discriminatory ability in both male and female patients. With all the results mentioned above, we may arrive at a preliminary conclusion that the ASDAS outperformed the other measures with respect to discriminatory ability in all different subgroups with different gender and different clinical manifestations.

We also analysed the correlation between the ASDAS and the acute inflammation score of MRI and compared the discriminatory power between them. It showed that the ASDAS outperformed MRI scores in correlating with patient global score, ESR and CRP, and in discriminating disease activity status in both AS and uSpA groups. The acute inflammation score of MRI correlated poorly with the other indices and had a relatively low discriminatory capacity. There were several possible reasons for it. The first one was: the score of MRI was a single index, which only took the inflammation of SI joint and spine into account. Therefore, it cannot reflect the whole spectrum of disease activity. Another reason may be: MRI, especially the lumbar MRI was only performed in patients with more established disease. The sample size was comparatively small. Some of the results for the MRI score were not clinically significant and had relatively low power. Further studies are still needed to confirm the result. Finally, it may be better to combine the acute inflammation score of SI joint and lumbar spine together, since neither of them alone could effectively represent the disease activity. However, even when we combined the two scores together, there were still thoracic and cervical vertebrae that we could not take into account. But it is not practical to scan the whole spine due to the high expense of MRI. The results above confirmed that the ASDAS outperformed the other measures in assessing disease activity in patients with AS and uSpA. Owing to the advantage, ASDAS is worth a wide clinical application.

In conclusion, our study showed that the new ASDAS versions are highly discriminatory measures of disease activity and efficacy following TNF- α inhibitor therapies in patients with AS and uSpAs in a Chinese population, showing a significant value in clinical practice.

Rheumatology key messages

- The ASDAS is a highly discriminatory disease activity measurement in patients with AS in China.
- The ASDAS can also be used in uSpA patients in China.

Acknowledgements

We gratefully acknowledge Profs Désirée van der Heijde, Louie James and David Yu for their constructive and professional suggestions in revising our manuscript. We thank all the patients for their cooperation during this study.

J.G. was supported by the grants of clinical subject (2007) of Ministry of Public Health of China and grants (2005A30801005) from Foundation of Guangdong province of China and 5010 Subject (2009–10) of Sun Yat-Sen University.

Disclosure statement: The authors have declared no conflicts of interest.

Supplementary data

Supplementary data are available at *Rheumatology* Online.

References

- Boonen A, Chorus A, Miedema H, van der Heijde D, van der Tempel H, van der Linden S. Employment, work disability and work days lost in patients with ankylosing spondylitis: a cross sectional study of Dutch patients. *Ann Rheum Dis* 2001;60:353–8.
- Braun J, Bollow M, Remlinger G *et al.* Prevalence of spondylarthropathies in HLA-B27 positive and negative blood donors. *Arthritis Rheum* 1998;41:58–67.
- Burgos-Vargas R. Undifferentiated spondyloarthritis: a global perspective. *Curr Rheumatol Rep* 2007;9:361–6.
- Garrett S, Jenkinson T, Kennedy LG, Whitelock H, Gaisford P, Calin A. A new approach to defining disease status in ankylosing spondylitis: the Bath Ankylosing Spondylitis Disease Activity Index. *J Rheumatol* 1994;21:2286–91.
- Rudwaleit M, van der Heijde D, Landewé R *et al.* The development of Assessment of SpondyloArthritis International Society classification criteria for axial spondyloarthritis (part II): validation and final selection. *Ann Rheum Dis* 2009;68:777–83.
- Braun J, Baraliakos X, Golder W *et al.* Magnetic resonance imaging examinations of the spine in patients with ankylosing spondylitis, before and after successful therapy with infliximab. *Arthritis Rheum* 2003;48:1126–36.
- Hermann KG, Braun J, Fischer T, Reissbauer H, Bollow M. Magnetic resonance tomography of sacroiliitis: anatomy, histological pathology, MR-morphology, and grading. *Radiologe* 2004;44:217–28.
- Maksymowych WP, Inman RD, Salonen D *et al.* Spondyloarthritis Research Consortium of Canada magnetic resonance imaging index for assessment of sacroiliac joint inflammation in ankylosing spondylitis. *Arthritis Rheum* 2005;53:703–9.
- Lukas C, Braun J, van der Heijde D *et al.* Scoring inflammatory activity of the spine by magnetic resonance imaging in ankylosing spondylitis: a multireader experiment. *J Rheumatol* 2007;34:862–70.
- Akdeniz O, Alayli G, Tosun FC *et al.* Early spondyloarthropathy: scintigraphic, biological, and clinical findings in MRI-positive patients. *Clin Rheumatol* 2008;27:469–74.
- Lukas C, Landewé R, Sieper J *et al.* Development of an ASAS-endorsed disease activity score (ASDAS) in patients with ankylosing spondylitis. *Ann Rheum Dis* 2009;68:18–24.
- van der Heijde D, Lie E, Kvien TK *et al.* The ASDAS is a highly discriminatory ASAS-endorsed disease activity score in patients with ankylosing spondylitis. *Ann Rheum Dis* 2009;68:1811–8.
- Van der Linden S, Valkenburg HA, Cats A. Evaluation of diagnostic criteria for ankylosing spondylitis. A proposal for modification of the New York criteria. *Arthritis Rheum* 1984;27:361–8.
- Dougados M, vanderLinden S, Juhlin R *et al.* The European Spondyloarthropathy Study Group preliminary criteria for the classification of spondyloarthropathy. *Arthritis Rheum* 1991;34:1218–27.
- Jones SD, Steiner A, Garrett SL. The Bath Ankylosing Spondylitis Patient Global Score (BAS-G). *Br J Rheumatol* 1996;35:66–71.
- Nakagawa S, Cuthill IC. Effect size, confidence interval and statistical significance: a practical guide for biologists. *Biol Rev* 2007;82:591–605.
- Spoorenberg A, van Tubergen A, Landewé R *et al.* Measuring disease activity in ankylosing spondylitis: patient and physician have different perspectives. *Rheumatology* 2005;44:789–95.
- Bakker C, Boers M, van der Linden S. Measures to assess ankylosing spondylitis: taxonomy, review and recommendations. *J Rheumatol* 1993;20:1724–30.
- Pedersen SJ, Sørensen IJ, Hermann KG *et al.* Responsiveness of the Ankylosing Spondylitis Disease Activity Score (ASDAS), and clinical and magnetic resonance imaging measures of disease activity in a 1 year follow-up study of patients with axial spondyloarthritis treated with TNF- α inhibitors. *Ann Rheum Dis* 2010;69:1065–71.