Arthritis Care & Research
Vol. 67, No. 1, January 2015, pp 74–79
DOI 10.1002/acr.22400

Is Spinal Mobility in Patients With Spondylitis Determined By Age, Structural Damage, and Inflammation?

JERUSALEM CALVO-GUTIERREZ,[1] JUAN L. GARRIDO-CASTRO,[2] JESUS GIL-CABEZAS,[2] CRISTINA GONZALEZ-NAVAS,[2] PILAR FONT UGALDE,[3] LORETO CARMONA,[4] AND EDUARDO COLLANTES-ESTEVEZ[5]

Objective. **To explore the association between mobility, inflammation, and structural damage in ankylosing spondylitis (AS).**
Methods. **Patients with AS were included in a cross-sectional study in which spinal mobility was measured by the Bath Ankylosing Spondylitis Metrology Index (BASMI) and by the University of Córdoba Ankylosing Spondylitis Metrology Index (UCOASMI), based on an automated motion analysis. Structural damage was measured by the modified Stoke Ankylosing Spondylitis Spine Score (mSASSS), and activity by the Ankylosing Spondylitis Disease Activity Score (ASDAS) and the Bath Ankylosing Spondylitis Disease Activity (BASDAI). We analyzed the correlations between variables, as well as interaction by multiple linear regression models to reach a predictive equation.**
Results. **Fifty AS patients, mainly men in their mid-40s and with moderate levels of disease activity and structural damage, were included in the study. BASMI and UCOASMI scores showed a strong correlation (r = 0.89). UCOASMI scores correlated stronger than BASMI with structural damage (r = 0.72 versus r = 0.67) and patient's age (r = 0.68 versus r = 0.56). Correlations of mobility were weaker with disease activity by the ASDAS (r = 0.38) and BASDAI (r = 0.49), and disease duration (r = 0.40). Multiple linear regression showed that factors associated to mobility by UCOASMI were age, the BASDAI, mSASSS, ASDAS (0:<2.1, 1:≥2.1), and disease duration >15 years. The largest weight in the equation corresponded to the mSASSS. The association between the ASDAS and UCOASMI is dependent on disease duration.**
Conclusion. **Mobility in AS is influenced by both structural damage and activity, but definitely also by age and disease duration. Improved mobility should be a relevant target in AS, even more prominently than activity, given its closer relation to structural damage.**

INTRODUCTION

Axial spondyloarthritis (AS) is a chronic degenerative rheumatic disease characterized by inflammatory back pain and consequent reduced spinal mobility. The assessment of spinal mobility is widely used in the followup of patients with AS (1,2). Most measures of spinal mobility are indirect, such as the finger to floor distance, and few, like the Schober test, are direct measures of spine flexibility. An assessment of the SpondyloArthritis International Society (ASAS) (3) recommends the following measures of spinal mobility for the followup of AS patients: thoracic expansion, modified Schober test, occipital-wall distance, cervical rotation, and lateral flexion. In addition, composite indices have been created, such as the Bath Ankylosing Spondylitis Metrology Index (BASMI) and its versions (4–6), which encompass several measures to produce a 0 to 10 score. The Edmonton Ankylosing Spondylitis Metrology Index (7) includes 4 items (cervical and hip rota-

Supported by several project grants from the I+D del Ministerio de Ciencia y Tecnología (DPI2006-02608), the Fondo de Investigación Sanitaria (FIS) from the Instituto de Salud Carlos III (PI08/90319), and Consejería de Salud de la Junta de Andalucía (PI- 0243).

[1]Jerusalem Calvo-Gutierrez, MD: Universitario Reina Sofia, and Maimonides Institute for Biomedical Research of Córdoba (IMIBIC), Córdoba, Spain; [2]Juan L. Garrido-Castro, PhD, Jesus Gil-Cabezas, MD, Cristina Gonzalez-Navas, RN: Maimonides Institute for Biomedical Research of Córdoba (IMIBIC), Córdoba, Spain; [3]Pilar Font Ugalde, MD, PhD: University of Córdoba, Córdoba, Spain; [4]Loreto Carmona, MD, PhD: Instituto de Salud Musculoesquelética, Madrid, Spain; [5]Eduardo Collantes-Estevez, MD, PhD: Universitario Reina Sofia, Maimonides Institute for Biomedical Research of Córdoba (IMIBIC), and University of Córdoba, Córdoba, Spain.

Address correspondence to Juan L. Garrido-Castro, PhD, Instituto Maimónides de Investigación Biomédica, Hospital Universitario Reina Sofía, Edificio Consultas Externas, Nivel-1 Avda. Menéndez Pidal s/n, 14004 Córdoba Spain. E-mail: cc0juanl@uco.es.

Submitted for publication March 31, 2014; accepted in revised form July 8, 2014.

Significance & Innovations

- Mobility in ankylosing spondylitis (AS) is influenced both by structural damage and activity, but definitely also by age and disease duration.
- Mobility should be a relevant target in AS, even more prominently than activity, given its closer relation to structural damage.
- Automated motion analysis provides a better noise-effect ratio in the measure of mobility than traditional measures.

tion, chest expansion, lateral lumbar flexion, and internal rotation of the hip), has good responsiveness, and simplifies the BASMI, but it is not widely used. However, all these measures depend on the observer and the use of a tape measure, and several authors have described a lack of precision, as well as poor reliability and sensitivity to change, which are most likely related to measurement error and noise (8–10). This is one of the main reasons why, despite the ample array of available measures and despite being considered a core measure, spinal mobility is not systematically included in clinical trials to assess response to treatment as other measures are. Among the 6 items evaluated in the ASAS (11), only the end point of lateral flexion proposes a measure of mobility.

Recently, automated motion capture systems have been applied to the field of measurement in AS. These systems allow a tridimensional measure of human mobility with higher levels of objectivity and precision than traditional measures (12). Our group has previously designed a motion capture system that can be used in patients with AS (13). In addition, we validated a metrologic index, the University of Córdoba Ankylosing Spondylitis Metrology Index (UCOASMI) (14), based on measures taken by the automated system. The UCOASMI has demonstrated higher reliability and better sensitivity to change than the BASMI, and although some feasibility issues remain (for a summary of the index, see Supplementary Appendix A, available in the online version of this article at http://onlinelibrary.wiley.com/doi/10.1002/acr.22400/abstract) (14), the UCOASMI reflects spinal mobility better than the BASMI. The BASMI includes intermalleolar distance among its measures. This measure is solely influenced by hip mobility, and hips are not evaluated in the modified Stoke Ankylosing Spondylitis Spine Score (mSASSS) or the Ankylosing Spondylitis Spinal Assessment by Magnetic Resonance Imaging (ASSpiMRI) score. Therefore, 20% of the information on mobility produced by the BASMI is not related to spinal mobility. In addition, the BASMI also includes tragus-to-wall distance, which is constant in long-term cases, while the UCOASMI evaluates neck and low-back regions in the 3 planes.

Both spinal inflammation and structural damage in the form of syndesmophytes and bony bridges are presumably the underlying causes of the reduced mobility. To measure structural damage in AS, the most widely used scoring system is the mSASSS (15,16). To measure inflammation, rheumatologists use the C-reactive protein (CRP) level, the erythrocyte sedimentation rate (ESR), and patient-reported questionnaires, such as the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) (17,18). Interestingly, the BASDAI, despite being a subjective measure, performs better than acute-phase reactants (19). The ASAS introduced the Ankylosing Spondylitis Disease Activity Score (ASDAS) to evaluate disease activity by combining several BASDAI items plus an objective measure, CRP level or ESR (20,21). The ASDAS demonstrated high responsiveness during treatment with tumor necrosis factor α inhibitors in patients with spondyloarthritis in several studies (22,23). Another way to measure inflammation, although restricted to studies and not to daily practice, is by the analysis of magnetic resonance images, with the ASspiMRI index (24).

A study by Machado et al underscores the presence of structural damage and of inflammation as sufficient to justify changes in mobility in patients with AS (25). In said study, mobility was measured by the BASMI, structural damage by the mSASSS, and inflammatory activity with the ASspiMRI (25). Another finding of Machado et al is that the associations to spinal mobility change by disease stage, being more influenced by spinal inflammation in early disease and by structural damage in later disease. Understanding the relationships between mobility and structural damage and inflammation would help us to better comprehend disease course in AS. Our study aims to explore the association between mobility, inflammation, and structural damage. The difference with previous studies is the use of a reliable system to measure mobility.

PATIENTS AND METHODS

We designed an observational, cross-sectional prospective study.

Patients. Eligible patients had to fulfill the New York modified criteria for AS (26). They were consecutively selected from an AS clinic from May to September 2012, and no exclusion criteria were established. Patients gave their informed consent to participate and the study was approved by the ethics committee of the hospital.

Spinal mobility. The BASMI was calculated in all patients from the following measures: finger-to-floor distance, lateral flexion, Schober test, thoracic expansion, intermalleolar distance, cervical rotation, occipital-wall distance, and tragus-to-wall distance.

In addition, we measured mobility with UCOTrack, an automated system based on the analysis of the information submitted by position markers placed on the patient (13). The patient is instructed to perform a series of movements (Figure 1) in front of 4 synchronized cameras working at 50 frames/second that register all kinematic information (13). The system analyzes range of motion in the 3 planes of neck and trunk. The UCOASMI is then calculated as a composite index that produces a score of cervical and spinal mobility based on serial kinematic measures (14). The score ranges from 0 to 10 (from best to worst mobility).

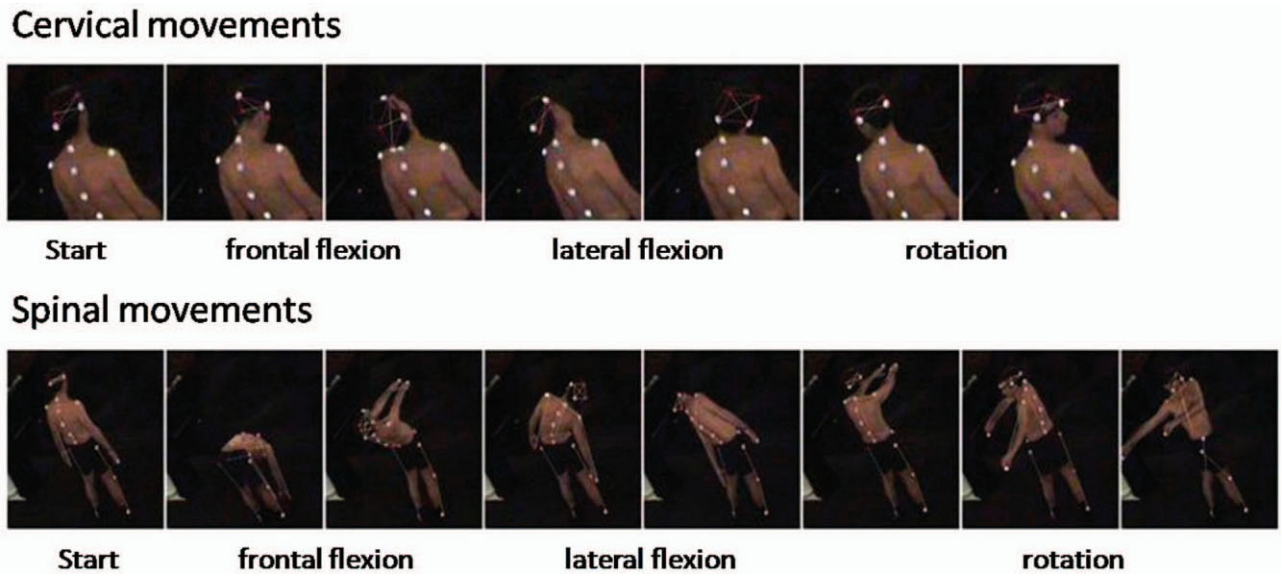

Figure 1. Movements performed by the patient as instructed for the neck (upper panels) and spine (lower panels) in the automated motion capture analysis. The automated system captures the distances between markers and location while in movement and produces the motion analysis.

Similar to the BASMI, the UCOASMI is derived from a selection of 5 individual measures (cervical flexion/extension, cervical rotation, trunk inclination during flexion and extension, lateral bending, and trunk rotation) based on metric properties and then calculated as a weighted average.

Other variables. In addition to the motion analysis and conventional mobility measurements, the following parameters were also recorded: weight and height, the BASDAI, the Ankylosing Spondylitis Quality of Life questionnaire, and the Bath Ankylosing Spondylitis Functionality Index.

Spinal radiographs were evaluated by an experienced radiologist (JC-G), blinded to the results of the other measures, who calculated the modified mSASSS. As to laboratory measures, the following were collected: HLA–B27, ESR, and CRP level. The ASDAS was then calculated from the results of the CRP level and several BASDAI items with the following formula: (0.121 × back pain) + (0.058 × duration of morning stiffness) + (0.110 × patient global) + (0.073 × peripheral pain/swelling) + (0.579 × lnCRP + 1) (21).

Data analysis. We described the patients through summary descriptive measures, i.e., absolute and relative frequencies for categorical variables and arithmetic mean and SD for normally distributed continuous variables. We used Pearson's correlation coefficient for the bivariate analysis. Then we ran multiple linear regression models to identify factors associated with mobility as measured by the UCOASMI. The variables entered in the model were age, BASDAI score, mSASSS total, ASDAS (0:>2.1, 1:≥2.1), and disease duration (0:<15 years, 1: ≥15 years). Previously, we ran bivariate analyses to select the variables for the final model with Student's *t*-test (variables with $P \geq 0.15$ were eliminated from the model). The scale of continuous variables was analyzed with the Box-Tidwell test. All possible interactions were evaluated. Variables with $P > 0.05$ were studied as potential confounding factors and were considered as such if the percentage of change in the coefficient was >20%. Collinearity was assessed through the variance inflation factor. Independency, normality, and residuals homoscedasticity were analyzed by the Durbin-Watson and Kolmogorov-Smirnov tests, and by plotting the residuals with the estimated values, respectively. Cook distance was used as a diagnostic test for extreme cases. R^2 was used to assess goodness of fit. All hypothesis tests were bilateral and were considered significant if P was less than 0.05. Data were managed and analyzed with SPSS, version 17.

RESULTS

Of the eligible patients, all accepted participation. Table 1 shows the descriptive data of the 50 patients included in the study. Patients were typical AS patients, mainly men in their mid-40s and in moderate levels of disease activity and structural damage. Twenty-eight percent of the patients had a CRP level >5 mg/dl and 38% had a disease for longer than 15 years.

Table 2 shows the correlations between the different measures and variables. The BASMI and UCOASMI showed a strong correlation as expected, as they both measure spinal mobility despite being based on a different set of measures ($r = 0.89$, $P < 0.001$). Correlation with other measures was similar for the UCOASMI and BASMI. The UCOASMI correlated well with structural damage ($r = 0.72$, $P < 0.001$) and patient's age ($r = 0.68$, $P < 0.001$). Correlations of the UCOASMI were weaker, although significant with disease activity by ASDAS ($r = 0.38$, $P < 0.001$), BASDAI ($r = 0.49$, $P < 0.001$), and disease duration ($r = 0.40$, $P < 0.001$). We found no correlation between CRP level and mobility.

Table 1. Description of a patient sample (n = 50) with axial spondyloarthritis*

Characteristics	Value
Men, no. (%)	36 (72)
Age, years	43.40 ± 10.76
Disease duration, years	15.66 ± 10.61
Body mass index, kg/m^2	27.89 ± 4.97
HLA–B27 positive, no. (%)	42 (84)
BASDAI	4.77 ± 2.53
BASFI	4.64 ± 2.96
ASQoL	4.42 ± 3.03
BASMI	3.57 ± 2.02
UCOASMI	5.26 ± 1.92
mSASSS	19.38 ± 20.62
CRP, mg/dl	5.73 ± 5.72
ASDAS	2.74 ± 1.08

Values are the mean ± SD unless indicated otherwise. BASDAI = Bath Ankylosing Spondylitis Disease Activity Index; BASFI = Bath Ankylosing Spondylitis Functionality Index; ASQoL = Ankylosing Spondylitis Quality of Life; BASMI = Bath Ankylosing Spondylitis Metrological Index; UCOASMI = University of Cordoba Ankylosing Spondylitis Metrological Index; mSASSS = modified Stoke Ankylosing Spondylitis Spinal Score; CRP = C-reactive protein; ASDAS = Ankylosing Spondylitis Disease Activity Score.

Multiple linear regression showed that factors associated with the UCOASMI were age, BASDAI, mSASSS, ASDAS (0:>2.1, 1:≥2.1), and disease duration >15 years. The ASDAS and disease duration showed a significant interaction, and so the interaction term was entered into the model. All assumptions for linear multiple regression were met (linearity and noncollinearity of independent variables, independency, normality, and homoscedasticity of residuals). No patient showed a Cook distance >1. Table 3 summarizes the linear regression and multiple linear regression results of factors associated to the UCOASMI. The largest weight in the equation corresponded to the mSASSS. The final predictive model for mobility was as follows: UCOASMI = 0.364 + (0.053 × age) + (0.052 × mSASSS) + (0.264 × BASDAI) + (0.766 × years of disease duration) + (0.664 × ASDAS) − (0.221 × [>15 years of disease duration × ASDAS]).

The association between the ASDAS and UCOASMI is dependent on disease duration. For a patient with a disease duration of <15 years, if the ASDAS is >2.1, the UCOASMI increases by 0.766, and when the ASDAS is ≤2.1, the UCOASMI decreases by 0.766 − 1.401 = −0.635. In addition, an increase in age of 5 years implies an increase of 5 × 0.053 = 0.265 UCOASMI units, and an increase of 5 mSASSS units implies an increase of 5 × 0.052 = 0.26 UCOASMI units.

We reran the models with the BASMI and with the individual components of the mobility indices, as well as with other measures produced by the motion capture system. In all cases, the models were worse in terms of R^2.

DISCUSSION

Our study shows that although spinal mobility may be driven by disease activity and structural damage, activity is not as closely related to structural damage as mobility. Therefore, spinal mobility may be a better surrogate for structural damage than activity and should be integrated in the measure of treatment response, perhaps over activity (11). The association between spinal mobility, structural damage, and inflammation in AS was already demonstrated by Machado et al (25). There are some differences, however, between the former study and ours. First, the mobility measure we used (14) has greater precision than the BASMI, which was used in the study by Machado et al. The BASMI, despite wide acceptance and use, is a measure with problems of reliability, variability, and precision. Madsen et al confirm a minimum detectable difference close to 1 (10).

This is one of the reasons why mobility as measured by the BASMI may not be systematically used in clinical trials to demonstrate short-term efficacy of interventions. In addition, it seems that the relationship between spinal mobility and both structural damage and activity is not simple, and 2 additional factors may modify it: age and disease duration. Notwithstanding, the BASMI includes occipital-wall distance, which is not included in the UCOASMI, and this measure is very specific for patients with large amounts of damage, and the relation with age may not be as evident. This may be another reason why Machado et al did not show age associated in their study.

It was not unexpected that age would have an influence on mobility, as we all experience this naturally (27,28). In fact, Chilton-Mitchell et al (29) found a difference in the BASMI in healthy individuals, from a mean 0.9 points in those age <25 years to a mean 2.1 in persons age >65 years. This is a relevant finding, as a study done in a

Table 2. Pairwise correlations between study variables and measures of mobility, structural damage, and disease activity in a sample of 50 patients with axial spondyloarthritis*

	BASMI	UCOASMI	mSASSS	ASDAS
Age	0.559†	0.676†	0.438†	0.231
Years of disease duration	0.245	0.396†	0.166	0.041
Body mass index, kg/m^2	0.294‡	0.364†	0.530†	0.176
BASDAI	0.464†	0.485†	0.099	0.850†
BASFI	0.586†	0.641†	0.387†	0.733†
ASQoL	0.326‡	0.380†	0.053	0.682†
CRP	0.006	0.015	0.051	0.535†
BASMI	–	0.887†	0.671†	0.364†
UCOASMI	0.887†	–	0.719†	0.384†
mSASSS	0.671†	0.719†	–	0.085
ASDAS	0.364†	0.384†	0.085	–

Values are the Pearson's r correlation coefficient. BASMI = Bath Ankylosing Spondylitis Metrological Index; UCOASMI = University of Cordoba Ankylosing Spondylitis Metrological Index; mSASSS = modified Stoke Ankylosing Spondylitis Spinal Score; ASDAS = Ankylosing Spondylitis Disease Activity Score; BASDAI = Bath Ankylosing Spondylitis Disease Activity Index; BASFI = Bath Ankylosing Spondylitis Functionality Index; ASQoL = Ankylosing Spondylitis Quality of Life; CRP = C-reactive protein.
† $P < 0.01$ (bilateral).
‡ $P < 0.05$ (bilateral).

Table 3. Factors associated with spinal mobility as measured by UCOASMI*

Variables	Bivariate analysis		Multivariate analysis, final model (R^2 = 00.813)		
	β coefficient (95% CI)	*P*	β coefficient (95% CI)	SC	*P*
Age, per year	0.12 (0.08, 0.16)	0.000	0.05 (0.02, 0.09)	0.30	0.002
mSASSS, per unit	0.07 (0.05, 0.09)	0.000	0.05 (0.04, 0.07)	0.55	0.000
BASDAI, per unit	0.37 (0.18, 0.56)	0.000	0.26 (0.11, 0.41)	0.35	0.001
Disease duration (>15 years)	10.35 (0.28, 20.42)	0.014	0.77 (0.55, 10.80)	0.20	0.033
ASDAS <20.1	−10.30 (−20.44, −0.15)	0.028	0.66 (−0.16, 10.49)	0.16	0.112
Disease duration × ASDAS	−10.53 (−40.30, 10.24)	0.259	−10.40 (−20.60, −0.20)	−0.22	0.023

* UCOASMI = University of Cordoba Ankylosing Spondylitis Metrological Index; 95% CI = 95% confidence interval; SC = standardized coefficients; mSASSS = modified Stoke Ankylosing Spondylitis Spinal Score; BASDAI = Bath Ankylosing Spondylitis Disease Activity Index; ASDAS = Ankylosing Spondylitis Disease Activity Score.

sample with younger individuals may have better baseline mobility than a study with older individuals.

In addition, disease duration, which in turn may be associated with age, was a plausible modifying factor. Disease duration reflects, in fact, the burden of disease activity in the long term, as well as how the disease was managed or how it responded to treatment. Therefore, disease duration is highly related to the accumulated activity and structural damage. This finding was also reflected in the study by Machado et al (25). Unfortunately, ours was not a longitudinal study and we could not answer the question whether one could predict structural damage in the long term by measuring mobility at a certain point in time. Wanders et al (30) were not able to predict structural damage by analyzing mobility, but perhaps if they had used a measure of mobility, such as the UCOASMI, they might have found it. We hypothesize so for 2 reasons. First, the UCOASMI has demonstrated a better effect-noise ratio than conventional measures of mobility (14). This may have an impact in confirming trends seen by other measures. For example, in the present study, BASMI correlations with the other measures were not as strong as those of the UCOASMI, which may be related to measure variability. Second, the UCOASMI includes an item with high validity but it cannot be easily measured without an automated motion capture system, namely trunk rotation (2).

Many questions remain unanswered. Is it possible to predict structural damage by changes in mobility? Is the reduction in mobility reflecting the progression to bony bridges? Do improvements in mobility change the radiologic course? The definitive study would be to demonstrate whether early intervention targeting improved mobility, through a combination of exercise (31) and pharmacologic therapy (32), has an effect on structural damage. Of course, given that inflammation reduces mobility, then inflammation must be targeted, but not solely. Mobility restrictions due to inflammation are temporary and occur during relapses of the disease. During inflammatory bouts, the target is clearly inflammation; but between episodes, antiinflammatory drugs may do little on mobility, or at least this needs to be tested.

In conclusion, mobility in AS is influenced by both structural damage and activity, but definitely also by age and disease duration. Since traditional measures of mobility are affected by a high noise-effect ratio, our proposal is to use sophisticated objective measures, such as automated motion analysis, at least for research.

ACKNOWLEDGMENT

We are grateful to the Ankylosing Spondylitis Patients' Association of Cordoba (ACEADE) for its collaboration in this study.

AUTHOR CONTRIBUTIONS

All authors were involved in drafting the article or revising it critically for important intellectual content, and all authors approved the final version to be submitted for publication. Dr. Calvo-Gutierrez had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study conception and design. Calvo-Gutierrez, Garrido-Castro, Gil-Cabezas, Gonzalez-Navas, Ugalde, Carmona, Collantes-Estevez.

Acquisition of data. Calvo-Gutierrez, Garrido-Castro, Gil-Cabezas, Gonzalez-Navas, Ugalde, Collantes-Estevez.

Analysis and interpretation of data. Calvo-Gutierrez, Garrido-Castro, Gil-Cabezas, Gonzalez-Navas, Ugalde, Collantes-Estevez.

REFERENCES

1. Sieper J, Rudwaleit M, Baraliakos X, Brandt J, Braun J, Burgos-Vargas R, et al. The Assessment of SpondyloArthritis international Society (ASAS) handbook: a guide to assess spondyloarthritis. Ann Rheum Dis 2009;Suppl 2:ii1–44.
2. Viitanen JV, Heikkila S, Kokko ML, Kautiainen H. Clinical assessment of spinal mobility measurements in ankylosing spondylitis: a compact set for follow-up and trials? Clin Rheumatol 2000;19:131–7.
3. Van der Heijde D, Calin A, Dougados M, Khan MA, van der Linden S, Bellamy N. Selection of instruments in the core set for DC-ART, SMARD, physical therapy, and clinical record keeping in ankylosing spondylitis: progress report of the ASAS Working Group. Assessments in Ankylosing Spondylitis. J Rheumatol 1999;26:951–4.
4. Jenkinson TR, Mallorie PA, Whitelock HC, Kennedy LG, Garrett SL, Calin A. Defining spinal mobility in ankylosing spondylitis (AS): the Bath AS Metrology Index. J Rheumatol 1994; 21:1694–8.
5. Jones SD, Porter J, Garrett SL, Kennedy LG, Whitelock H, Calin A. A new scoring system for the Bath Ankylosing Spondylitis Metrology Index (BASMI). J Rheumatol 1995;22:1609.
6. Van der Heijde D, Landewe R, Feldtkeller E. Proposal of a linear definition of the Bath Ankylosing Spondylitis Metrology Index (BASMI) and comparison with the 2-step and 10-step definitions. Ann Rheum Dis 2008;67:489–93.
7. Maksymowych WP, Mallon C, Richardson R, Conner-Spady

B, Jauregui E, Chung C, et al. Development and validation of the Edmonton Ankylosing Spondylitis Metrology Index. Arthritis Rheum 2006;55:575–82.
8. Martindale JH, Sutton CJ, Goodacre L. An exploration of the inter- and intra-rater reliability of the Bath Ankylosing Spondylitis Metrology Index. Clin Rheumatol 2012;31:1627–31.
9. Auleley GR, Benbouazza K, Spoorenberg A, Collantes E, Hajjaj-Hassouni N, van der Heijde D, et al. Evaluation of the smallest detectable difference in outcome or process variables in ankylosing spondylitis. Arthritis Rheum 2002;47:582–7.
10. Madsen OR, Hansen LB, Rytter A, Suetta C, Egsmose C. The Bath Metrology Index as assessed by a trained and an untrained rater in patients with spondylarthropathy: a study of intra- and inter-rater agreements. Clin Rheumatol 2009;28:35–40.
11. Brandt J, Listing J, Sieper J, Rudwaleit M, van der Heijde D, Braun J. Development and preselection of criteria for short term improvement after anti-TNF α treatment in ankylosing spondylitis. Ann Rheum Dis 2004;63:1438–44.
12. Castro JL, Medina-Carnicer R, Galisteo AM. Design and evaluation of a new three-dimensional motion capture system based on video. Gait Posture 2006;24:126–9.
13. Garrido-Castro JL, Medina-Carnicer R, Schiottis R, Galisteo AM, Collantes-Estevez E, Gonzalez-Navas C. Assessment of spinal mobility in ankylosing spondylitis using a video-based motion capture system. Man Ther 2012;17:422–6.
14. Garrido-Castro JL, Escudero A, Medina-Carnicer R, Galisteo AM, Gonzalez-Navas C, Carmona L, et al. Validation of a new objective index to measure spinal mobility: the University of Cordoba Ankylosing Spondylitis Metrology Index (UCOASMI). Rheumatol Int 2014;34:401–6.
15. Creemers MC, Franssen MJ, van't Hof MA, Gribnau FW, van de Putte LB, van Riel PL. Assessment of outcome in ankylosing spondylitis: an extended radiographic scoring system. Ann Rheum Dis 2005;64:127–9.
16. Wanders AJ, Landewe RB, Spoorenberg A, Dougados M, van der Linden S, Mielants H, et al. What is the most appropriate radiologic scoring method for ankylosing spondylitis? A comparison of the available methods based on the Outcome Measures in Rheumatology Clinical Trials filter. Arthritis Rheum 2004;50:2622–32.
17. Dougados M, Gueguen A, Nakache JP, Velicitat P, Zeidler H, Veys E, et al. Clinical relevance of C-reactive protein in axial involvement of ankylosing spondylitis. J Rheumatol 1999;26:971–4.
18. 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.
19. Spoorenberg A, van der Heijde D, de Klerk E, Dougados M, de Vlam K, Mielants H, et al. Relative value of erythrocyte sedimentation rate and C-reactive protein in assessment of disease activity in ankylosing spondylitis. J Rheumatol 1999;26:980–4.
20. Machado P, Landewe R, Lie E, Kvien TK, Braun J, Baker D, et al. Ankylosing Spondylitis Disease Activity Score (ASDAS): defining cut-off values for disease activity states and improvement scores. Ann Rheum Dis 2011;70:47–53.
21. Van der Heijde D, Lie E, Kvien TK, Sieper J, van den Bosch F, Listing J, et al. ASDAS, a highly discriminatory ASAS-endorsed disease activity score in patients with ankylosing spondylitis. Ann Rheum Dis 2009;68:1811–8.
22. Pedersen SJ, Sorensen IJ, Hermann KG, Madsen OR, Tvede N, Hansen MS, et al. Responsiveness of the Ankylosing Spondylitis Disease Activity Score (ASDAS) and clinical and MRI measures of disease activity in a 1-year follow-up study of patients with axial spondyloarthritis treated with tumour necrosis factor α inhibitors. Ann Rheum Dis 2010;69:1065–71.
23. Xu M, Lin Z, Deng X, Li L, Wei Y, Liao Z, et al. 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. Rheumatology (Oxford) 2011;50:1466–72.
24. Braun J, Baraliakos X, Golder W, Brandt J, Rudwaleit M, Listing J, et al. Magnetic resonance imaging examinations of the spine in patients with ankylosing spondylitis, before and after successful therapy with infliximab: evaluation of a new scoring system. Arthritis Rheum 2003;48:1126–36.
25. Machado P, Landewe R, Braun J, Hermann KG, Baker D, van der Heijde D. Both structural damage and inflammation of the spine contribute to impairment of spinal mobility in patients with ankylosing spondylitis. Ann Rheum Dis 2010;69:1465–70.
26. 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.
27. McGregor AH, McCarthy ID, Hughes SP. Motion characteristics of the lumbar spine in the normal population. Spine (Phila Pa 1976) 1995;20:2421–8.
28. Van Herp G, Rowe P, Salter P, Paul JP. Three-dimensional lumbar spinal kinematics: a study of range of movement in 100 healthy subjects aged 20 to 60+ years. Rheumatology (Oxford) 2000;39:1337–40.
29. Chilton-Mitchell L, Martindale J, Hart A, Goodacre L. Normative values for the Bath Ankylosing Spondylitis Metrology Index in a UK population. Rheumatology (Oxford) 2013;52:2086–90.
30. Wanders A, Landewe R, Dougados M, Mielants H, van der Linden S, van der Heijde D. Association between radiographic damage of the spine and spinal mobility for individual patients with ankylosing spondylitis: can assessment of spinal mobility be a proxy for radiographic evaluation? Ann Rheum Dis 2005;64:988–94.
31. O'Dwyer T, O'Shea F, Wilson F. Exercise therapy for spondyloarthritis: a systematic review. Rheumatol Int 2014;34:887–902.
32. Schoels MM, Braun J, Dougados M, Emery P, Fitzgerald O, Kavanaugh A, et al. Treating axial and peripheral spondyloarthritis, including psoriatic arthritis, to target: results of a systematic literature search to support an international treat-to-target recommendation in spondyloarthritis. Ann Rheum Dis 2014;73:238–42.