UCSF UC San Francisco Previously Published Works

Title

Regional radiographic damage and functional limitations in patients with ankylosing spondylitis: Differences in early and late disease

Permalink https://escholarship.org/uc/item/37d8p5fg

Journal Arthritis Care & Research, 65(2)

ISSN 2151-464X

Authors

Ward, Michael M Learch, Thomas J Gensler, Lianne S <u>et al.</u>

Publication Date

2013-02-01

DOI

10.1002/acr.21821

Peer reviewed



NIH Public Access

Author Manuscript

Arthritis Care Res (Hoboken). Author manuscript; available in PMC 2014 February 01

Published in final edited form as:

Arthritis Care Res (Hoboken). 2013 February ; 65(2): 257–265. doi:10.1002/acr.21821.

REGIONAL RADIOGRAPHIC DAMAGE AND FUNCTIONAL LIMITATIONS IN PATIENTS WITH ANKYLOSING SPONDYLITIS: DIFFERENCES IN EARLY AND LATE DISEASE

Michael M. Ward, MD, MPH,

Intramural Research Program, National Institute of Arthritis and Musculoskeletal and Skin Diseases, National Institutes of Health, Bethesda, MD

Thomas J. Learch, MD,

Department of Radiology, Cedars-Sinai Medical Center, Los Angeles, CA

Lianne S. Gensler, MD, Division of Rheumatology, University of California-San Francisco, CA

John C. Davis Jr., MD, MPH, Current address: Genentech, South San Francisco, CA

John D. Reveille, MD, and Division of Rheumatology and Clinical Immunogenetics, University of Texas Health Sciences Center at Houston, Houston, TX

Michael H. Weisman, MD Division of Rheumatology, Cedars-Sinai Medical Center, Los Angeles, CA

Abstract

Objective—Radiographic damage and functional limitations both increase with the duration of ankylosing spondylitis (AS). We examined whether radiographic damage contributed more to functional limitations in late AS than in early AS, and if the strength of association varied with the anatomic region of damage.

Methods—In this cross-sectional study of 801 patients with AS, we examined associations of the lumbar modified Stoke AS Spine Score (mSASSS), cervical mSASSS, lumbar posterior fusion, cervical posterior fusion, and hip arthritis with the Bath AS Functional Index (BASFI) and the Health Assessment Questionnaire (HAQ-S).

Results—Higher lumbar and cervical mSASSS were associated with more functional limitations, but there was an interaction between mSASSS and the duration of AS such that the strength of their association with functional limitations decreased with increasing duration of AS. Cervical posterior fusion was associated with worse functioning independent of mSASSS. Hip arthritis was significantly associated with functional limitations independent of measures of spinal damage. Among patients with AS 40 years, the number of comorbid conditions accounted for most of the variation in functioning. Results were similar for both the BASFI and HAQ-S.

Conclusions—Although both radiographic damage and functional limitations increase over time in AS, the relative contribution of radiographic damage to functional limitations is lower among patients with longstanding AS than early AS, suggesting patients may accommodate to limited

Address for correspondence: Dr. Michael Ward, NIAMS/NIH, Building 10 CRC, Room 4-1339, 10 Center Drive, Bethesda, MD 20892-1468. Telephone (301) 496-7263; Facsimile (301) 480-8882; wardm1@mail.nih.gov.

flexibility. Damage in different skeletal regions impacts functioning over the duration of AS. Functional limitations due to comorbidity supervene in late AS.

Keywords

Ankylosing spondylitis; radiographic damage; functional limitations

Limitations in physical functioning, including problems with self-care, mobility, and instrumental activities of daily living, tend to increase with the duration of many chronic musculoskeletal diseases, often as a consequence of progressive joint damage, deconditioning, advancing age, and comorbidity. In ankylosing spondylitis (AS), functional limitations are more common in patients with more long-standing disease (1–10). These limitations have largely been attributed to reduced spinal flexibility due to vertebral fusion. Breathing restriction, hip arthritis, peripheral arthritis, and AS activity may also contribute (11–13). Supporting this concept are studies demonstrating that the extent of spinal fusion increases with the duration of AS (12–20) and is correlated with the degree of functional limitation (11,13,15–17,21,22). In the World Health Organization International Classification of Functioning (WHO/ICF) framework, these represent associations between alterations in body structure, reflected by radiographic changes, and difficulties in activity and participation (23).

Although it is commonly assumed that functional limitations in longstanding AS are related to more advanced spinal fusion, studies directly examining whether radiographic damage plays a larger role in functional limitations in long-standing AS than in early AS have not been reported. Because lumbar spine damage typically precedes cervical spine and hip involvement, the relationship between radiographic damage and physical function may change over the duration of AS, as different skeletal regions become affected (13,20). It is not known how functional limitations in AS evolve in relation to radiographic damage in different spinal regions. Radiographic measures of spinal damage such as the modified Stoke AS Spine Score (mSASSS) are most heavily weighted by syndesmophyte formation, and focus exclusively on changes in the anterior vertebral bodies. Fusion of vertebral facet joints also impairs spinal mobility, and might impact physical functioning (24–27).

We examined the association between radiographic damage and functional limitations in a large cohort of patients with AS to address three questions: Does the strength of association between radiographic damage and functional limitations vary over the duration of AS? What are the relative contributions of lumbar spine, cervical spine, and hip damage to functional limitations over the duration of AS? Is fusion of lumbar or cervical facet joints associated with functional limitations, independent of changes in the vertebral bodies?

METHODS

Patients

Patients were participants in the Prospective Study of Outcomes in AS (PSOAS), an observational study of predictors of AS severity (7). Patients were recruited from the investigators' clinics, patient support groups, and the community. Patients were at least 18 years old and had a diagnosis of AS by the modified New York criteria (28). All had pelvic and spinal radiographs to confirm their diagnosis, and completed questionnaires about their medical histories. The study protocol was approved by the institutional review board at each site, and all patients provided written informed consent. Enrollment began in 2002 and is continuing.

Patients who were enrolled and whose radiographs had been scored as of March 2011 were eligible for inclusion in this cross-sectional analysis. Of 879 patients, we excluded 13 who had spinal surgery, 7 who had incomplete radiographs, 54 with poor visualization of three or more anterior vertebral corners, and 4 with missing data on the Bath AS Functional Index (BASFI), leaving 801 patients.

Measures

We used the BASFI as the main measure of functional limitations. The BASFI is a 10-item questionnaire on which respondents rate the degree of difficulty they have performing specific tasks, using visual analog scales with anchors of 0 (easy) and 100 (impossible) (29). The index is calculated as the mean of the 10 responses. The BASFI has good reliability and construct validity (15,16,21,22,29). We used the Health Assessment Questionnaire modified for the Spondyloarthropathies (HAQ-S) as a second measure, to determine if similar associations would be found irrespective of the specific measure of functional limitations. The HAQ-S is a 25-item questionnaire on which respondents rate the degree of difficulty (0 = no difficulty to 3 = unable to do) they have performing tasks in 10 functional areas (30). The total score is the average of the highest score in the 10 areas. The HAQ-S also has good reliability and construct validity (30,31).

The independent variables of interest were five measures of radiographic damage. We used the lumbar and cervical spine scores of the modified Stoke AS score (mSASSS) as separate measures to test if functional limitations differed with the severity of involvement in each region (24). The lumbar mSASSS and cervical mSASSS can each range from 0 (no abnormalities) to 36 (complete fusion). The mSASSS assesses changes in the anterior vertebral bodies but not the posterior elements. Because we were interested in possible associations with facet joint fusion, we scored lateral films of the lumbar spine and cervical spine as to whether facet joints were not fused at any level, fused at some levels, or fused at all levels. In preliminary analyses, there were only minor differences in associations with incomplete facet joint fusion and those with no fusion, and therefore for the analysis we classified patients as having facet joint fusion at all lumbar levels or not, or at all cervical levels or not. Lastly, we used the Bath AS Radiology Index (BASRI)-hip score to measure hip damage (32). The BASRI-hip is an ordinal rating of joint space narrowing, erosions, or osteophytes in the hip (0 - 4). Hip deformity, bone apposition, and hip replacements are scored as 4. We used the average score of both hips in the analyses.

A single musculoskeletal radiologist (TJL) scored all radiographs for posterior fusion and BASRI-hip, as well as mSASSS for 52% of patients. Intra-reader reliabilities, based on the films of 50 patients, exceeded 0.96 for each of the five radiographic measures. Two rheumatologists (MMW and MHW) scored the mSASSS for the remaining patients. Inter-reader reliabilities were 0.96 for the cervical mSASSS and 0.97 for the lumbar mSASSS, based on the films of 26 patients.

Other variables included age, sex, ethnicity (white versus other), and five characteristics previously associated with functional limitations in this cohort: education level, number of comorbid conditions, current smoking, lifetime occupational activity score, and AS in a first-degree relative (7). Duration of AS was calculated from the onset of persistent musculoskeletal symptoms.

Statistical Analysis

We used Spearman correlations to examine associations between lumbar mSASSS, cervical mSASSS, posterior lumbar fusion, posterior cervical fusion, and BASRI-hip and the BASFI (and HAQ-S) in the entire cohort and in subgroups stratified by decade of AS (0 to 9.9

years; 10.0 to 19.9 years; 20.0 to 29.9 years; 30.0 to 39.9 years, and 40.0 years or longer). We used multiple linear regression analysis to examine the association between radiographic scores and functional measures, adjusting for the covariates noted above (sex, ethnicity, education level, current smoking, number of comorbid conditions, lifetime occupational physical activity score, and history of AS in a first-degree relative). Age and duration of AS were highly collinear, and we used duration of AS in the models. To determine if the association between radiographic damage and functional limitation varied over the duration of AS, we tested interactions between each radiographic measure and the duration of AS. Lastly, we used multiple linear regression analysis to test the association between each regional score and functional limitations within subgroups by decade of AS. These regression analyses provided the partial r^2 for each regional radiographic score, which represents the proportion of variation in the functional measure associated with the radiologic score, adjusted for the other variables in the model. Scores on the BASFI and HAQ-S were positively skewed, so we used their square root transformations as the dependent variables in the regression models. We used SAS programs version 9.2 (SAS Institute, Cary, NC) for analysis.

RESULTS

Patient characteristics

The 801 patients varied in age and duration of AS (Table 1). Seventy-nine percent were white, and 85% were HLA-B27 positive. Comorbid conditions increased with the duration of AS, with the most common being iritis (34.7%), hypertension (23.3%), depression (15.2%), peptic ulcer disease (12.5%), and asthma (9.3%). Cardiovascular disease, osteoporosis, diabetes mellitus, and cancer were more common in those with longstanding AS (Supplemental table 1). Radiographic damage in the lumbar spine, cervical spine, and hip increased progressively with the duration of AS, but substantial variation was present among patients in each decade. Seventy-two percent of patients in the first decade and 5% of patients in the fifth decade had a lumbar mSASSS of 0, while 23% in the fifth decade had complete anterior lumbar fusion (mSASSS = 36). Similarly, 65% of patients in the first decade and 12% of patients in the fifth decade had a cervical mSASSS of 0, while 34% in the fifth decade had complete anterior cervical fusion (mSASSS = 36). Lumbar posterior fusion was associated with lumbar anterior fusion: 94% of patients with a lumbar mSASSS of 36 had lumbar posterior fusion, but these accounted for only 48% of patients with lumbar posterior fusion. Similarly, 72% of patients with a cervical mSASSS of 36 had cervical posterior fusion, and these accounted for 64% of those with cervical posterior fusion. Correlations among the other radiographic measures were varied (Supplemental table 2). Across decades, proportions with any radiographic hip damage were 23.1%, 32.5%, 36.7%, 47.8%, and 42.6%. BASFI and HAQ-S were higher among patients with longer durations of AS.

Association between radiographic measures and functional limitations

In univariate analyses, more severe radiographic damage in each region was associated with higher BASFI scores. Correlation of the BASFI with lumbar mSASSS was 0.35, cervical mSASSS was 0.37, lumbar posterior fusion was 0.31, cervical posterior fusion was 0.33, and BASRI-hip was 0.23 (all p < .0001). In multivariate analysis, lumbar mSASSS, cervical mSASSS, cervical posterior fusion, and BASRI-hip scores were associated with BASFI, while lumbar posterior fusion was not (Table 2). Cervical mSASSS and BASRI-hip had the strongest associations with BASFI, but cervical posterior fusion had an additional independent association with BASFI. There was no evidence of multicollinearity among the radiographic measures.

To test if the strength of associations between radiographic scores and BASFI varied over the duration of AS, we added interaction terms between each radiographic score and duration of AS in sequential models (Table 2). There was a significant interaction between lumbar mSASSS and duration of AS (p = .003), and between cervical mSASSS and duration of AS (p = .02), with the negative coefficients indicating that the strength of association between both mSASSS scores and BASFI decreased as the duration of AS increased. Figure 1 demonstrates these relationships graphically. The BASFI was higher among those with longer durations of AS and among those with higher lumbar and cervical mSASSS, but the association was stronger when the duration of AS was shorter (i.e. the plane was steeper), and less strong as the duration of AS increased. For example, at 10 years of AS, the estimated mean difference in BASFI between patients with a lumbar mSASSS of 5 (who had a mean BASFI of 18.2) and patients with a lumbar mSASSS of 30 (who had a mean BASFI of 25.7) was 7.5. In contrast, at 40 years of AS, the estimated mean difference in BASFI between patients with lumbar mSASSS of 5 and 30, respectively, was only 0.2, all other factors held constant.

There were no significant interactions between lumbar posterior fusion, cervical posterior fusion, or BASRI-hip scores and duration of AS in their associations with the BASFI (Table 2). Because lumbar posterior fusion may be difficult to detect, we repeated the analyses omitting this measure. Results were nearly identical, and significant interactions between the duration of AS and lumbar mSASSS (p = .003) and cervical mSASSS (p = .02) remained. There were no significant interactions between sex and lumbar mSASSS (p = .85), cervical mSASSS (p = .24), or BASRI-hip scores (p = .46) in association with the BASFI.

Relative contributions of lumbar spine, cervical spine, and hip radiographic damage to functional limitations over the duration of AS

To investigate further how the relationship between regional radiographic damage and functional limitations changes over the duration of AS, we examined associations by decade of AS. Among patients with AS < 10 years, lumbar mSASSS and lumbar posterior fusion were correlated with BASFI, but cervical spine and hip scores were not (Table 3). Lumbar mSASSS was more strongly associated with BASFI among patients in decades 2 and 3 than in decade 5, the group with the highest BASFI scores. Cervical mSASSS and cervical posterior fusion were more highly correlated with BASFI than were lumbar scores in decades 3 and 4. Hip scores demonstrated the strongest correlation with BASFI in decade 4.

In multivariate analyses adjusting for potential confounding factors, lumbar mSASSS and lumbar posterior fusion together accounted for 2.3% of the variation in BASFI in decade 1 and 2.6% of variation in BASFI scores in decade 2, but much smaller and non-significant associations with BASFI in decades 3, 4 and 5 (Figure 2). Cervical mSASSS and BASRI-hip accounted for 6.5% and 4.1% of the variation in BASFI in decade 3, but cervical mSASSS had weaker associations later in AS. Hip damage accounted for much more of the variation in BASFI than spinal damage in decade 4 (12.7%). In decade 5, the combined contribution of radiographic scores to variation in the BASFI (1.8%) was much less than that of comorbid conditions (12.1%). All models were statistically significant (p < .0001) with model R² of .21, .25, .37, .47, and .36 for decades 1 – 5, respectively.

Associations with HAQ-S

The associations between regional radiographic damage and HAQ-S were similar to those for the BASFI, with significant interactions between the duration of AS and both the lumbar mSASSS and cervical posterior fusion. The pattern of associations by decade of AS were also similar (Supplemental table 3 and Supplemental figure 1).

DISCUSSION

In this large cohort of patients with AS, more severe radiographic damage was associated with more severe functional limitations. The strength of association was similar to previous studies, which reported correlations from 0.24 to 0.45 (11,13,16,17,21). However, we did not find that radiographic spinal damage contributed more to functional limitations in late AS than in early AS. In contrast, the strength of association decreased in late AS. Although lumbar spine damage was most prevalent and severe in the fourth and fifth decades, lumbar damage contributed little to the variation in functional limitations among patients with late AS. Lumbar spine damage contributed most to limitations in the first two decades and later waned, as demonstrated by the significant interaction between anterior lumbar spine scores and duration of AS. As cervical spine damage became more prevalent in the third and fourth decades, it contributed more to variation in functional limitations, but was also weaker among patients with longer durations of AS than those with shorter durations. Results were similar for two measures of functional limitations that assessed different activities and had different response formats, which strengthens the validity of the findings.

What can account for this observation? Associations may be weak if there was little variation in radiographic scores. However, there was substantial variation in the mSASSS across durations of AS and among patients with similar durations of AS. There was also no evidence of a ceiling effect in the BASFI or HAQ-S, which might have decreased associations among those with longstanding AS. Another possible explanation is that the model fit was poorer among patients with longstanding AS, but coefficients of determination were higher for models for the fourth and fifth decade subgroups. Alternatively, the questionnaires may have been poor at capturing limitations common among patients with longstanding AS. This may occur if the functions asked about were less relevant to persons with longstanding AS, or if the questionnaires missed functions that often had a major impact on functioning in late AS. However, similar associations were found with two different measures of physical function, and both asked primarily about activities of daily living.

An alternative explanation for the decreased strength of association between lumbar and cervical mSASSS and functional limitations with longer durations of AS is that patients accommodated to their spinal damage. Early in AS, when lumbar involvement was modest but new, lumbar damage had a greater impact than in late AS, when lumbar damage was more extensive but also more long-standing. A similar interpretation may apply to cervical spine damage, which had its strongest association with functional limitations in the second and third decades, and decreased thereafter. Because cervical involvement develops later than lumbar involvement, accommodation to it would be expected to occur later in the duration of AS.

Most patients with complete anterior cervical fusion also had posterior cervical fusion, but not all patients with complete posterior cervical fusion had advanced anterior cervical changes. Radiographic changes in the anterior and posterior cervical spine in AS are associated, although the specificity of the association differs among studies (18, 33). In our study, patients with posterior cervical fusion had more functional limitations than those without posterior cervical fusion, independent of damage in the anterior cervical spine. These findings are consistent with the major role of facet joints in neck mobility, and highlight the importance of assessing facet joints to obtain a more complete understanding of the relationship between spinal damage and functioning in AS. In contrast, posterior lumbar fusion was not independently associated with functional limitations. This may be because movement at other joints such as the hips can compensate for fusion in these joints. Their oblique orientation makes it more difficult to assess fusion of lumbar facet joints, and readings may have greater measurement error.

Hip arthritis has been recognized as a poor prognostic feature in AS, but it has not been considered as prominently as spinal disease as a cause of functional limitation in AS (3–5,12,13,15,17,34–38). Although patients with hip arthritis are more likely to have more severe spinal arthritis (13,15,20), the association of hip arthritis and functional limitations in our study was independent of radiographic spinal damage. Our findings suggest that hip arthritis has a more prominent role than spinal damage in functional limitations among patients with long-standing AS. Hip arthritis may also limit one's ability to compensate for an inflexible lumbar spine, and so may exaggerate functional limitations.

Comorbidity was the most important correlate among patients with more than 40 years of AS. This may reflect both an increased prevalence of comorbid conditions and a different set of conditions with a greater impact on functioning (39,40). Comorbidity may also be a surrogate of physical frailty, which can contribute to functional limitations. Many previous studies of functional limitations in AS have not examined the impact of comorbidity, but in our cohort, comorbid conditions have consistently been a strong predictor of physical functioning (7). This association may be more prominent among cohorts with more longstanding AS.

The strengths of this study include a large sample, high reliability of radiographic scores, examination of regional skeletal abnormalities, and use of two measures of functional limitations. However, our study has some limitations. The duration of AS was based on patient recall, which might have been inaccurate in some cases. However, misclassification would not be expected to alter trends in associations by duration of AS. Alterations in body structure other than radiographic damage and alterations in body function also impact activity and participation in patients with AS (41), and may have different effects in patients with early or late disease. We did not collect information on peripheral arthritis or AS activity for all patients, and cannot determine how much these may have contributed to functional limitations. We recognize that structural damage affects physical function by first leading to impairments in movement, but we chose to examine the direct association between skeletal changes and physical function rather than intermediate pathways. These factors, along with environmental and personal factors, may contribute to the variation in functioning we observed. We examined patients who met modified New York criteria for AS; patients evolving to AS are unlikely to have spinal damage and therefore are less informative for this study. Lastly, we can only infer that accommodation to functional limitations imposed by spinal damage occurred over time. To test this directly, longitudinal studies are needed, but such studies would need to follow patients for decades.

Our results indicate that anterior lumbar and cervical spine damage, posterior cervical spine fusion, and hip arthritis each contribute to functional limitations in patients with AS. However, the strength of this association with anterior lumbar damage and anterior cervical damage decreases, rather than increases, with the duration of AS. Anterior lumbar spinal damage as measured by the mSASSS has its strongest association with functional limitations in early, rather than late, AS, while cervical spinal damage has its most prominent association with functional limitations in mid-to-late AS. This pattern suggests that patients may accommodate to some aspects of spinal involvement over time. The prominent role of hip damage suggests that a focus on assessing and aggressively treating hip arthritis throughout the duration of AS may represent an important way to decrease functional limitations. In late AS, functional limitations due to spinal or hip arthritis may be eclipsed by those due to comorbidity, emphasizing the need to include measures of comorbidity when examining predictors of functional limitations in patients with AS.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

This work was supported by NIH/NIAMS PO-1-052915, NIH RO1-AR048465, Cedars-Sinai GCRC MO1-RR00425, University of Texas at Houston GCRC M01-RR02558, The Rosalind Russell Center for Arthritis Research at The University of California San Francisco, and the Intramural Research Program, National Institute of Arthritis and Musculoskeletal and Skin Diseases, NIH. We thank Lori Guthrie, Felice Lin, Stephanie Brown, Stephanie Morgan, Vera Wirawan, and Laura Diekman for their assistance.

References

- Taylor AL, Balakrishnan C, Calin A. Reference centile charts for measures of disease activity, functional impairment, and metrology in ankylosing spondylitis. Arthritis Rheum. 1998; 41:1119– 25. [PubMed: 9627023]
- Guillemin F, Brainçon S, Pourel J, Gaucher A. Long-term disability and prolonged sick leaves as outcome measurements in ankylosing spondylitis. Possible predictive factors. Arthritis Rheum. 1990; 33:1001–6. [PubMed: 2369416]
- 3. Abbott CA, Helliwell PS, Chamberlain MA. Functional assessment in ankylosing spondylitis: evaluation of a new self-administered questionnaire and correlation with anthropometric variables. Br J Rheumatol. 1994; 33:1060–6. [PubMed: 7981994]
- Gran JT, Skomsvoll JF. The outcome of ankylosing spondylitis: a study of 100 patients. Br J Rheumatol. 1997; 36:766–71. [PubMed: 9255111]
- Dalyan M, Güner A, Tuncer S, Bilgiç A, Arasil T. Disability in ankylosing spondylitis. Disabil Rehabil. 1999; 21:74–9. [PubMed: 9990492]
- Zink A, Braun J, Listing J, Wollenhaupt J. German Collaborative Arthritis Centers. Disability and handicap in rheumatoid arthritis and ankylosing spondylitis—results from the German Rheumatological database. J Rheumatol. 2000; 27:613–22. [PubMed: 10743798]
- Ward MM, Weisman MH, Davis JC Jr, Reveille JD. Risk factors for functional limitations in patients with long-standing ankylosing spondylitis. Arthritis Rheum. 2005; 53:710–7. [PubMed: 16208654]
- Stone M, Warren RW, Bruckel J, Cooper D, Cortinovis D, Inman RD. Juvenile-onset ankylosing spondylitis is associated with worse functional outcomes than adult-onset ankylosing spondylitis. Arthritis Rheum. 2005; 53:445–51. [PubMed: 15934110]
- 9. Kobelt G, Andlin-Sobocki P, Maksymowych WP. Costs and quality of life of patients with ankylosing spondylitis. J Rheumatol. 2006; 33:289–95. [PubMed: 16465660]
- Tam L-S, Chang K-Y, Li EK. The influence of illness and variables associated with functional limitations in Chinese patients with ankylosing spondylitis. J Rheumatol. 2007; 34:1032–9. [PubMed: 17343322]
- Landewé R, Dougados M, Meilants H, van der Tempel H, van der Heijde D. Physical function in ankylosing spondylitis is independently determined by both disease activity and radiographic damage of the spine. Ann Rheum Dis. 2009; 68:863–7. [PubMed: 18628283]
- Boonen A, van der Cruyssen B, de Vlam K, Steinfeld S, Ribbens C, Lenaerts J, et al. Spinal radiographic changes in ankylosing spondylitis: Associations with clinical characteristics and functional outcome. J Rheumatol. 2009; 36:1249–55. [PubMed: 19447933]
- Chen H-A, Chen C-H, Liao H-T, Lin Y-J, Chen P-C, Chen W-S, et al. Factors associated with radiographic spinal involvement and hip involvement in ankylosing spondylitis. Semin Arthritis Rheum. 2011; 40:552–8. [PubMed: 20870274]
- Calin A, Mackay K, Santos H, Brophy S. A new dimension to outcome: application of the Bath Ankylosing Spondylitis Radiology Index. J Rheumatol. 1999; 26:988–92. [PubMed: 10229434]
- Doran M, Brophy S, Mackay K, Taylor G, Calin A. Predictors of longterm outcome in ankylosing spondylitis. J Rheumatol. 2003; 30:316–20. [PubMed: 12563688]

Ward et al.

- 16. Salaffi F, Carotti M, Garofalo G, Giuseppetti GM, Grassi W. Radiological scoring methods for ankylosing spondylitis: a comparison between the Bath Ankylosing Spondylitis Radiology Index and the modified Stoke Ankylosing Spondylitis Spine Score. Clin Exp Rheumatol. 2007; 25:67– 74. [PubMed: 17417993]
- Kaya T, Gelal F, Gunaydin R. The relationship between severity and extent of spinal involvement and spinal mobility and physical functioning in patients with ankylosing spondylitis. Clin Rheumatol. 2006; 25:835–9. [PubMed: 16391887]
- Lee JY, Kim JI, Park JY, Choe JY, Kim CG, Chung SH, et al. Cervical spine involvement in longstanding ankylosing spondylitis. Clin Exp Rheumatol. 2005; 23:331–6. [PubMed: 15971420]
- El Maghraoui A, Bensabbah R, Bahiri R, Bezza A, Guedira N, Hajjaj-Hassouni N. Cervical spine involvement in ankylosing spondylitis. Clin Rheumatol. 2003; 22:94–8. [PubMed: 12740671]
- 20. Jang JH, Ward MM, Rucker AN, Reveille JD, Davis JC Jr, Weisman MH, et al. Ankylosing spondylitis: Patterns of radiographic involvement a re-examination of accepted principles in a cohort of 769 patients. Radiology. 2011; 258:192–8. [PubMed: 20971774]
- 21. Spoorenberg A, van der Heijde D, de Klerk E, Dougados M, de Vlam K, Mielants H, et al. A comparative study of the usefulness of the Bath Ankylosing Spondylitis Functional Index and the Dougados Functional Index in the assessment of ankylosing spondylitis. J Rheumatol. 1999; 26:961–5. [PubMed: 10229428]
- 22. Bostan EE, Borman P, Bodur H, Barça N. Functional disability and quality of life in patients with ankylosing spondylitis. Rheumatol Int. 2003; 23:121–6. [PubMed: 12739042]
- Boonen A, Maksymowych WP. Measurement: function and mobility (focusing on the ICF framework). Best Pract Res Clin Rheumatol. 2010; 24:605–24. [PubMed: 21035083]
- 24. 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 scoing system. Ann Rheum Dis. 2005; 64:127–9. [PubMed: 15051621]
- Russell AS, Jackson F. Computer assisted tomography of the apophyseal changes in patients with ankylosing spondylitis. J Rheumatol. 1986; 13:581–5. [PubMed: 3735280]
- Simkin PA, Downey DJ, Kilcoyne RF. Apophyseal arthritis limits lumbar motion in patients with ankylosing spondylitis. Arthritis Rheum. 1988; 31:798–802. [PubMed: 3382452]
- Viitanen JV, Kokko M-L, Lehtinen K, Suni J, Kautiainen H. Correlation between mobility restrictions and radiologic changes in ankylosing spondylitis. Spine. 1995; 20:492–6. [PubMed: 7747236]
- Goei The HS, Steven MM, van der Linden SM, Cats A. Evaluation of diagnostic criteria for ankylosing spondylitis: a comparison of the Rome, New York, and modified New York criteria in patients with a positive clinical history screening test for ankylosing spondylitis. Br J Rheumatol. 1985; 24:242–9. [PubMed: 3160423]
- Calin A, Garrett S, Whitelock H, Kennedy LG, O'Hea J, Mallorie P, et al. A new approach to defining functional ability in ankylosing spondylitis: the development of the Bath Ankylosing Spondylitis Functional Index. J Rheumatol. 1994; 21:2281–5. [PubMed: 7699629]
- Daltroy LH, Larson MG, Roberts NW, Liang MH. A modification of the Health Assessment Questionnaire for the spondyloarthropathies. J Rheumatol. 1990; 17:946–50. [PubMed: 2213762]
- Ward MM, Kuzis S. Validity and sensitivity to change of spondylitis-specific measures of functional disability. J Rheumatol. 1999; 26:121–7. [PubMed: 9918252]
- 32. MacKay K, Brophy S, Mack C, Doran M, Calin A. The development and validation of a radiographic grading system for the hip in ankylosing spondylitis: the Bath Ankylosing Spondylitis Radiology hip index. J Rheumatol. 2000; 27:2866–72. [PubMed: 11128678]
- de Vlam K, Mielants H, Veys EM. Involvement of the zygopophyseal joint in ankylosing spondylitis: relation to the bridging syndesmophyte. J Rheumatol. 1999; 26:1738–45. [PubMed: 10451071]
- 34. Amor B, Santos RS, Nahal R, Listrat V, Dougados M. Predictive factors for the longterm outcome of spondyloarthropathies. J Rheumatol. 1994; 21:1883–7. [PubMed: 7837155]
- 35. Robertson LP, Davis MJ. A longitudinal study of disease activity and functional status in a hospital cohort of patients with ankylosing spondylitis. Rheumatology. 2004; 43:1565–8. [PubMed: 15353608]

- Brophy S, Calin A. Ankylosing spondylitis: interaction between genes, joints, age at onset, and disease expression. J Rheumatol. 2001; 28:2283–8. [PubMed: 11669170]
- 37. Boonen A, Chorus A, Miedema H, van der Heijde D, Landew R, Schouten H, et al. Withdrawal from the labour force due to work disability in patients with ankylosing spondylitis. Ann Rheum Dis. 2001; 60:1033–9. [PubMed: 11602474]
- Falkenbach A, Franke A, van der Linden S. Factors associated with body function and disability in patients with ankylosing spondylitis: a cross-sectional study. J Rheumatol. 2003; 30:2186–92. [PubMed: 14528516]
- 39. Kang JH, Chen YH, Lin HC. Comorbidity profiles among patients with ankylosing spondylitis: a nationwide population-based study. Ann Rheum Dis. 2010; 69:1165–8. [PubMed: 20375121]
- Bremander A, Petersson IF, Bergman S, Englund M. Population-based estimates of common comorbidities and cardiovascular disease in ankylosing spondylitis. Arthritis Care Res. 2010; 63:550–6.
- Dagfinrud H, Kjeken I, Mowinckel P, Hagen KB, Kvien TK. Impact of functional impairment in ankylosing spondylitis: Impairment, activity limitation, and participation restrictions. J Rheumatol. 2005; 32:516–23. [PubMed: 15742446]

SIGNIFICANCE

- This is the first study to examine associations between radiographic damage in individual anatomic regions and functional limitations in patients with ankylosing spondylitis (AS).
- Lumbar spine damage has less influence on functional limitations in late AS than in early AS, despite being more common and more severe in late AS.
- Hip arthritis and comorbidity are major contributors to functional limitations in late AS.

Ward et al.



Figure 1.

Association between the lumbar modified Stoke Ankylosing Spondylitis Spine Score (mSASSS) (A), cervical modified Stoke Ankylosing Spondylitis Spine Score (B) and duration of ankylosing spondylitis with the Bath Ankylosing Spondylitis Functional Index (BASFI). The duration of AS is plotted on the x axis, the mSASSS on the y axis, and the BASFI on the z (vertical) axis. Surfaces were computed based on mulitivariate models that also included age, sex, ethnicity, education level, current smoking, number of comorbid conditions, occupational activity score, and family history of ankylosing spondylitis as covariates. In each figure, the BASFI increased with longer durations of AS and higher mSASSS readings, but the association between mSASSS and BASFI was stronger when the duration of AS was short (i.e. the plane was steeper), and became less strong at longer durations (i.e. the plane was almost flat).



Figure 2.

Proportion of variation explained (Partial r^2) by lumbar mSASSS (solid red), lumbar posterior fusion (striped red), cervical mSASSS (solid blue), cervical posterior fusion (striped blue), hip scores (yellow), and number of comorbid conditions (purple) in models predicting the Bath Ankylosing Spondylitis Functional Index. Separate models were created for patients in each decade of duration of ankylosing spondylitis. Additional variables in each model were age, sex, ethnicity, education level, current smoking, occupational activity score, and family history of ankylosing spondylitis.

Table 1

Characteristics of all patients and patient subgroups by decade of duration of ankylosing spondylitis. Values are percentages or median (25th percentile, 75th percentile).*

			Duration of	Ankylosing Spondy	/litis (years)	
	All	0.9 - 0.9	10.0 - 19.9	20.0 - 29.9	30.0 - 39.9	40.0 and longer
Number	801	200	164	219	117	101
Age, years	46.0 (34.2, 56.4)	30.2 (24.1, 37.5)	36.7 (32.0, 42.3)	47.9 (43.2, 54.7)	55.0 (52.0, 60.0)	65.4 (60.8, 70.8)
Duration of AS, years	20.7 (10.0, 31.8)	4.9 (2.2, 7.3)	15.3 (12.4, 17.9)	24.1 (21.3, 27.2)	34.5 (32.5, 36.8)	45.0 (41.4, 50.2)
% men	73.3	64.0	75.6	75.3	79.5	76.2
% white	79.0	69.5	73.8	79.5	86.3	0.79
Education level, years	16 (14, 18)	16 (14, 17)	16 (14, 18)	16 (14, 18)	16 (14, 18)	16 (14, 18)
% current smoker	12.6	15.0	18.3	11.4	8.6	6.9
% with AS in a first degree relative	21.1	18.0	18.9	20.6	27.3	24.7
Occupational physical activity $\dot{\tau}$	2.0 (1.1, 2.2)	2.0 (1.4, 2.4)	2.0 (1.2, 2.3)	2.0 (1.0, 2.2)	2.0 (1.1, 2.1)	2.0 (1.2, 2.3)
Number of comorbid conditions						
% with 0	18.2	35.0	21.3	13.7	7.7	2.0
% with 1	26.1	33.0	30.0	26.0	22.2	10.9
% with 2	22.4	15.5	25.6	28.3	21.4	18.8
% with 3 or more	33.3	16.5	23.1	32.0	48.7	68.3
Lumbar mSASSS (0 – 36)	3.0 (0, 14.4)	$0\ (0,\ 1)$	2.0 (0, 10.0)	5.0 (0, 15.3)	10.0 (2.0, 30.0)	15.0 (4.0, 32.0)
Cervical mSASSS (0 – 36)	4.8 (0, 25.2)	0 (0, 2.7)	2.2 (0, 10.0)	10.0 (2.4, 31.0)	24.0 (5.4, 36.0)	25.2 (6.0, 36.0)
Lumbar posterior fusion (%)	19.5	2.5	15.2	19.6	34.2	42.6
Cervical posterior fusion (%)	17.6	1.5	7.9	23.7	34.2	32.7
BASRI hip $(0-4)$	0 (0, 1)	$0\ (0,\ 0)$	$0\ (0,\ 1)$	0 (0, 1)	0 (0, 2)	$0\ (0,1.5)$
BASFI (0 – 100)	29.6 (13.7, 54.5)	21.2 (8.2, 44.2)	23.7 (12.7, 44.5)	34.1 (16.5, 61.0)	33.8 (20.7, 56.7)	43.3 (21.1, 68.0)
HAQ-S (0 – 3)	0.5 (0.2, 1.0)	$0.4\ (0.1,\ 0.9)$	$0.4\ (0.1,\ 0.8)$	0.6 (0.3, 1.2)	0.6 (0.2, 1.2)	0.7~(0.3, 1.4)

Arthritis Care Res (Hoboken). Author manuscript; available in PMC 2014 February 01.

* AS = ankylosing spondylitis. BASR1 = Bath Ankylosing Spondylitis Radiology Index. BASF1 = Bath Ankylosing Spondylitis Functional Index. HAQ-S = Health Assessment Questionnaire modified for the Spondyloarthropathies.

 $\dot{\tau}$ Mean patient-reported physical activity in all current and past jobs (1 = little; 2 = moderate; 3 = heavy), weighed by the number of years in each job.

Table 2

NIH-PA Author Manuscript

Association of regional radiographic damage scores and the Bath Ankylosing Spondylitis Functional Index, by multiple linear regression analysis.*

	Bas	seline mo	del		Mod	els includi	ng interac	tions	
	Beta	t	d	Beta	t	þ	Beta	t	þ
Lumbar mSASSS	0.019	1.96	50.	0.053	3.55	.0004	0.019	1.99	.05
Cervical mSASSS	0.034	4.07	<.0001	0.032	3.81	.0002	0.058	4.59	<.0001
Lumbar posterior fusion	-0.072	-0.26	08.	0.037	0.016	06.	-0.034	-0.12	.91
Cervical posterior fusion	0.563	2.18	:03	0.619	2.41	.02	0.659	2.54	.02
BASRI-hip	0.318	4.45	<.0001	0.323	4.55	<.0001	0.320	4.50	<.0001
Lumbar mSASSS \times duration	-	-		-0.001	-2.98	.003	-		-
Cervical mSASSS \times duration				-	ı		-0.001	-2.52	.02

		Models ii	ncluding i	nteraction	s				
	Beta	t	d	Beta	t	d	Beta	t	d
Lumbar mSASSS	0.020	2.08	.04	0.019	2.00	.05	0.019	1.97	.05
Cervical mSASSS	0.032	3.89	.0001	0.033	3.97	<.0001	0.034	4.06	<.0001
Lumbar posterior fusion	0.625	1.29	.20	-0.051	-0.18	.86	-0.062	-0.22	.83
Cervical posterior fusion	0.610	2.36	.02	1.35	2.54	.02	0.574	2.22	.02
BASRI-hip	0.324	4.54	<.0001	0.319	4.48	<.0001	0.382	2.66	600.
Lumbar posterior fusion \times duration	-0.024	-1.77	80.	-	-	-	-	-	
Cervical posterior fusion \times duration				-0.026	-1.69	.10	-	-	
$BASRI-hip \times duration$							-0.002	-0.52	.61
*									

⁷Adjusted for duration of AS, sex, ethnicity, education level, current smoking, number of comorbid conditions, lifetime occupational physical activity score, and history of AS in a first-degree relative. The dependent variable was square root of BASFI.

Table 3

Correlations between measures of radiographic damage and the Bath Ankylosing Spondylitis Functional Index among subgroups by decade of duration of ankylosing spondylitis. $^{\not{\tau}}$

Radiographic Measure 0 - 9:9 10.0 - 19:9 20.0 - 29:9 40.0 Lumbar mSASSS .25 ** .33 *** .31 *** .24 * 40.0 Cervical mSASSS .10 .28 ** .41 *** .33 ** 74 * Cervical mSASSS .10 .28 ** .41 *** .33 ** 74 * Lumbar posterior fusion .18 .26 ** .29 *** .33 ** 74 * Cervical mSASSS .10 .28 ** .31 *** .33 ** 74 * Umbar posterior fusion .18 .26 ** .29 *** .33 ** 74 ** BASRI-hip .11 .25 ** .34 *** .39 *** 75 *** .37 ***			Duration o	of Ankylosing	Spondylitis (ye	ears)
Lumbar mSASS .25 ** .31 *** .24 * Lumbar mSASSS .10 .28 ** .41 *** .24 * Cervical mSASSS .10 .28 ** .41 *** .33 ** Lumbar posterior fusion .18 * .26 ** .31 *** .33 ** Cervical mSASSS .10 .28 ** .31 *** .33 ** Lumbar posterior fusion .18 * .26 ** .33 *** .33 ** BASRI-hip .11 .25 ** .34 *** .39 ***	Radiographic Measure	0 - 9.9	10.0 - 19.9	20.0 - 29.9	30.0 - 39.9	40.0 and longer
Cervical mSASSS .10 .28 ** .41 *** .33 ** Lumbar posterior fusion .18 * .26 ** .29 *** .33 ** Cervical posterior fusion .11 .25 ** .34 *** .39 *** BASRI-hip .16 * .09 .26 *** .37 ***	Lumbar mSASSS	.25 **	.33 ***	.31 ***	.24 *	.26 *
Lumbar posterior fusion .18 * .26 ** .29 *** .33 ** Cervical posterior fusion .11 .25 ** .34 *** .39 *** BASRI-hip .16 * .09 .26 *** .37 ***	Cervical mSASSS	.10	.28 **	*** It.	.33 **	.34 *
Cervical posterior fusion .11 .25 ** .34 *** .39 *** BASRI-hip .16 * .09 .26 *** .37 ***	Lumbar posterior fusion	.18 *	.26 **	.29 ***	.33 **	.28 *
BASRI-hip .16 * .09 .26 *** .37 ***	Cervical posterior fusion	.11	.25 **	.34 ***	.39 ***	.26 *
	BASRI-hip	.16 *	60.	.26 ***	.37 ***	.17

 $\dot{ au}$ mSASSS = modified Stoke Ankylosing Spondylitis Spine Score; BASRI = Bath Ankylosing Spondylitis Radiology Index

p < .05;p < .001;p < .001; *** p < .0001