

Repeated Spinal Mobility Measures and Their Association With Radiographic Damage in Ankylosing Spondylitis

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Objective. We sought to explore the relationship between changes in repeated mobility measures and spinal structural progression in patients with ankylosing spondylitis (AS) over time.

Methods. We studied patients with AS from the PSOAS (Prospective Study of Outcomes in AS) cohort and performed longitudinal multivariable regression modeling to assess the relationship of structural damage measured by their regional (cervical or lumbar) modified Stoke AS Spinal Score (mSASSS) and selected cervical (eg, cervical rotation, lateral bending, and occiput-to-wall distance) and lumbar spinal mobility measures (eg, Schöber's test and lumbar lateral bending) that were collected at least every 2 years from 2003 to 2019.

Results. The median length of follow-up for our 518 patients with cervical mSASSS measurements and 573 with lumbar mSASSS measurements was 4.08 (interquartile range [IQR] 2.25–6.67) and 4.17 (IQR 2.25–6.67) years, respectively. Among the mobility measures, based on multivariable regression models adjusting for clinical/demographic variables and C-reactive protein, we did not observe meaningful associations between changes in spinal mobility with their respective regional mSASSS. Baseline mSASSS, male sex, increased C-reactive protein (CRP), and longer disease duration were associated with increased longitudinal mSASSS in all analyses.

Conclusion. Our study shows that 2-year changes in individual spinal mobility measures are not reliably associated with increased, longitudinal, AS-related spinal structural progression. We also confirmed the relationship of baseline mSASSS, sex, CRP, and disease duration with AS-related structural spinal progression over time.

INTRODUCTION

Spinal mobility is clearly a highly visible and clinically important (particularly to the patient) aspect of ankylosing spondylitis (AS) (1); thus, measures of spinal mobility have been routinely used and

endorsed as a core outcome measure by the Assessment of Spondyloarthritis International Society (ASAS) and Outcome Measures in Rheumatology (OMERACT) group for clinical trials and clinical care (2). However, the prognostic abilities of repeated measures of spinal mobility have not been sufficiently clarified in either the clinical or

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SIGNIFICANCE & INNOVATIONS

- Worsened cervical and lumbar spinal mobility measure changes within patients were not associated with greater spinal structural disease over time.

research domain. It has been suggested that early spinal mobility abnormalities may predict spinal fusion (3). Although some studies reported associations between individual mobility measures of the cervical and lumbar spine and the extent of spine radiographic damage, other studies reported weak or no correlations (4–7). Mobility measure indices such as the Bath AS Metrology Index have shown correlation with radiographic spinal severity (8).

In addition, sociodemographic and clinical factors, such as age, sex, ethnicity, height, and body mass index, have been associated with loss of spinal mobility (9). Furthermore, disease-specific factors, such as spinal inflammation, have also been associated with overall spinal mobility changes (10–12). This juxtaposition has been noted in clinical trials with stable or improved mobility measures despite radiographic progression (13).

Understanding the relationships between changes in mobility measures and spinal structural damage over time could help substantiate the clinical utility of such mobility measures in AS if changes in measures were shown to be prognostic. We examined the relationship between changes in individual mobility measures and radiographic structural progression over time in a large well-characterized cohort of patients with AS in whom spinal mobility measures were consistently performed.

PATIENTS AND METHODS

Patients. Patients were participants in the PSOAS (Prospective Study of Outcomes in AS), a longitudinal observational study of patients with AS. Entry criteria for this cohort include being 18 years of age or older and meeting the modified New York Criteria for AS (14). Patients were recruited from the investigators' clinics, patient support groups (such as the Spondylitis Association of America), and community rheumatologists. Patients were included from the following five study sites: Cedars-Sinai Medical Center in Los Angeles, California; the University of Texas Health Science Center at Houston; the National Institutes of Health Clinical Center; the University of California at San Francisco; and the Princess Alexandra Hospital in Brisbane, Australia. Each institution had the study approved by their respective institutional review boards, and each participating subject reviewed and signed an informed consent form.

Clinical assessments. Clinical information was obtained by reviewing medical records, administering questionnaires, and by performing structured study visits every 4 to 6 months. Sex, age, educational status, ethnicity (self-reported), date of axial symptom onset, date of enrollment (when consent to participate was signed),

disability status, and history of comorbidities, including uveitis, psoriasis, inflammatory bowel disease, or other musculoskeletal disorders, were recorded. Medication use and family history of spondyloarthritis were also queried. Instruments completed by the patients included self-reported pain on a visual analog scale, Bath AS Disease Activity Index (BASDAI), global health (Patient Global Assessment), and functional limitations as measured by the Bath AS Functional Index (BASFI) (15,16). C-reactive protein (CRP) and erythrocyte sedimentation rate were measured at each visit.

Radiographs of the lumbar spine (anterior–posterior and lateral) and cervical spine (lateral) were taken at the baseline visit and every 2 years to assess structural severity/progression using the modified Stoke AS Spinal Score (mSASSS) (17). The mSASSS is the preferred ASAS/OMERACT radiograph measure used to assess structural progression (18). The mSASSS is scored as the sum of the numerical scores for the anterior corners of the cervical spine from the lower border of C2 to the upper border of T1, and the anterior corners of the lumbar spine from the lower border of T12 to the upper border of S1 (a total of 24 corners). Each vertebral corner is scored as follows: 0 = normal; 1 = erosions, sclerosis, or squaring; 2 = nonbridging syndesmophytes; 3 = bridging syndesmophytes. The total score range is 0 to 72. The mSASSS for each radiographic set was based on readings by a central, expert musculoskeletal radiologist (TJL) and a second, study site expert rheumatologist experienced in AS research. Radiographs were read in sequence at a patient level. TJL was blinded to all clinical aspects of the patient's record, including treatment. All mSASSS values underwent further quality assurance by the PSOAS Data Management and Statistical Core, with a published substudy showing strong inter-rater reliability (IRR) and intrarater reliability (intraclass correlation coefficient [ICC]) in PSOAS mSASSS values, as follow: IRR = 0.90 (95% confidence interval [CI] 0.82-0.94) and ICC = 0.83 (95% CI 0.72-0.90) (19). Discrepancies between the two readers and/or serial readings were adjudicated by a third investigator (JDR).

Spinal mobility measures were performed at each study visit by the study visit investigators. Of the measurements of physical impairment recorded in the PSOAS (20), the following individual mobility tests were selected for study given their hypothesized relationship with regional cervical or lumbar mSASSS: cervical rotation, cervical lateral flexion, occiput-to-wall (OTW) distance, lumbar flexion (eg, Schöber's test), and lateral lumbar bending. Cervical rotation and cervical lateral flexion were recorded as the sum of maximal right and left movements, using a protractor. We measured OTW distance, Schöber's test, and lateral lumbar bending using a tape measure. The reliability of these individual measures is excellent, with interobserver reliability ranging from 0.90 (cervical lateral flexion) to 0.98 (lateral lumbar flexion) and intraobserver reliability ranging from 0.96 (cervical flexion) to 0.99 (Schöber's test) in previous studies (21). All visits and repeat spinal mobility measures were performed by the study site investigators or physical therapists trained in spinal metrology.

Statistical analysis. Independent associations of cervical and lumbar spinal mobility measures with corresponding regional (cervical or lumbar) mSASSSs were examined in longitudinal negative binomial regression modeling using a generalized estimating equation that accounts for within-patient correlation and distribution of data. Specifically, we conducted longitudinal data analyses with regional cervical and lumbar mSASSSs as the dependent variables, separately. Corresponding individual spinal mobility measures were the independent variables of interest in each longitudinal regional mSASSS analysis. We first tested the association between quartiles of the metrology measure and regional mSASSS. We then separately tested the association between change (defined as increased, decreased, and/or no change in comparison with the immediate prior clinical visit) in metrology measures with change in regional mSASSS. In our multivariable modeling, we adjusted for the spinal mobility assessor(s) by study site as well as clinical/demographic variables (ie, age, sex, smoking status, baseline regional mSASSS, longitudinal BASDAI, longitudinal CRP levels, Patient Global Assessment, nonsteroidal anti-inflammatory drugs, and tumor necrosis factor inhibitors). All time-variant covariables were examined at the same study visit as the interval mSASSS outcome. Possible confounders and effect modifiers were examined by testing all first-order interactions between the spinal mobility measure and the covariables included in our final models. We conducted sensitivity analyses by right-censoring the patient when they had a regional mSASSS (cervical or lumbar) of 32 or greater and 34 or greater in separate analyses. Additionally, in sensitivity analyses, we also applied minimal detectable change/smallest detectable difference (SDD) reference values when available (22–24). All analyses were performed at a 5% level of significance using SAS 9.4 (SAS Institute).

RESULTS

We analyzed and reported data for all patients for whom all baseline variables (more than one set of radiographs to assess progression as well as appropriate clinical spinal mobility measures) were obtained. Follow-up was available in 518 patients with cervical mSASSS measurements and 573 with lumbar mSASSS measurements (median length of follow-up of 4.08 (interquartile range [IQR] 2.25-6.67) and 4.17 (IQR 2.25-6.67) years, respectively). The main reason for the discrepancy between the number of cervical and lumbar spinal mSASSS assessments was that, if the regional mSASSS had already reached the maximum score (complete fusion), further radiographs were not obtained. Table 1 shows the baseline sociodemographic, clinical, and spinal imaging parameters of the study population. The relationships between clinical/laboratory factors were explored in univariable analyses. Disease duration, male sex, current smoking, CRP, increased BASFI and greater than 10 years’ disease duration showed associations with increased mSASSSs (data not shown).

Table 1. Summary of baseline clinical, demographic, and imaging characteristics of study population of cervical lumbar analyses

Characteristics	Cervical (n = 518)	Lumbar (n = 542)
Male, n (%)	392 (75.68)	409 (75.46)
White, n (%)	419 (80.89)	438 (80.81)
Education > high school, n (%)	420 (81.08)	437 (80.62)
Number of X-ray sets, median (IQR)	3 (2-4)	3 (2-4)
Follow-up, median (IQR), yr	4.08 (2.25-6.67)	4.17 (2.25-6.67)
Age at baseline, mean (SD), yr	41.73 (13.42)	42.20 (13.45)
Disease duration at baseline, median (IQR), yr	14.00 (6.00-24.50)	15.00 (7.00-26.00)
Number of comorbidities, median (IQR)	2.00 (1.00-3.00)	2.00 (1.00-3.00)
Baseline BASFI score (1-100), median (IQR)	22.70 (9.20-44.00)	23.70 (9.40-45.40)
Baseline BASDAI score (1-10), median (IQR)	3.20 (1.60-5.39)	3.25 (1.57-5.39)
First observed CRP, median (IQR), mg/dl	0.40 (0.20-0.98)	0.40 (0.20-1.03)
First observed ESR, median (IQR), mm/h	10.00 (5.00-20.00)	11.00 (5.00-21.00)
Baseline mSASSS, median (IQR)	2.00 (0.00-14.00)	2.00 (0.00-8.00)
Baseline occiput-to-wall test, median (IQR), cm	0.00 (0.00-6.00)	-
Baseline cervical lateral flexion, median (IQR), cm	58.50 (30.00-75.00)	-
Baseline cervical rotation, median (IQR), degrees	105.0 (75.00-130.0)	-
Baseline Schöber’s test, median (IQR), cm	-	3.45 (2.00-4.50)
Baseline lateral lumbar bend, median (IQR), cm	-	24.00 (15.00-33.50)

BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Spondylitis Functional Index; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; IQR, interquartile range; mSASSS, modified Stoke Ankylosing Spondylitis Spinal Score.

Longitudinal associations between spinal mobility measures and mSASSS.

Longitudinal associations of mSASSSs and absolute spinal mobility values based on multivariable longitudinal regression models were carried out while controlling for potential confounding variables (Table 2). The average adjusted change per year in mean (±SD) was 0.77 (±3.69) for the cervical mSASSS and 0.70 (±3.24) for the lumbar mSASSS (Figure 1). Spinal mobility data were categorized into quartiles because they exhibited a nonlinear association with mSASSS. Worse spinal mobility quartiles for each of the five measures was associated with increased mSASSS values. Baseline regional mSASSS, male sex, elevated CRP, and disease duration showed significant associations with longitudinal mSASSS in all spinal mobility analyses. No significant effect modifiers (such as an interaction between spinal mobility and smoking) were found while building our multivariable models.

Table 2. Multivariable analyses of longitudinal mSASSS and absolute spinal mobility measures

Variable	Adjusted Rate Ratio (95% Confidence Interval)				
	Lateral Lumbar Bend ^a (n = 542)	Schöber's Test ^b (n = 542)	Occiput-to-Wall Distance ^c (n = 518)	Lateral Cervical Bend ^d (n = 518)	Cervical Rotation ^e (n = 518)
Spinal mobility measure					
Most restricted (0-25 th percentile); reference	1.00	1.00	1.00	1.00	1.00
25th-50th percentile vs. ≤25th percentile	0.71 (0.59-0.85)*	0.94 (0.81-1.09)	0.91 (0.82-1.02)	0.81 (0.71-0.93)*	0.76 (0.66-0.87)*
50th-75th percentile vs. ≤25th percentile	0.49 (0.38-0.63)*	0.85 (0.71-1.01)	0.86 (0.76-0.96)*	0.66 (0.60-0.78)*	0.57 (0.48-0.67)*
Least restricted >75th percentile vs. ≤25th percentile	0.38 (0.28-0.52)*	0.83 (0.69-0.99)*	0.86 (0.76-0.96)*	0.61 (0.53-0.74)*	0.54 (0.45-0.65)*
Baseline mSASSS	1.11 (1.10-1.12)*	1.11 (1.10-1.12)*	1.11 (1.10-1.12)*	1.11 (1.10-1.12)*	1.11 (1.10-1.11)*
Male vs. female	1.85 (1.34-2.54)*	1.84 (1.34-2.54)*	2.53 (1.78-3.60)*	2.36 (1.68-3.312)*	2.31 (1.66-3.22)*
Disease duration at baseline ≥20 yr vs. <20 yr	1.02 (1.01-1.03)*	1.02 (1.01-1.03)*	1.05 (1.03-1.06)*	1.04 (1.03-1.05)*	1.04 (1.03-1.05)*
Exercise (≥120 min/wk vs. <120 min/wk) ^f	1.02 (0.90-1.16)	1.03 (0.91-1.16)	0.98 (0.94-1.02)	0.96 (0.92-1.01)	0.96 (0.90-1.01)
Smoking (current vs. other)	1.44 (1.00-2.07)*	1.50 (1.05-2.14)*	0.91 (0.66-1.27)	0.96 (0.70-1.31)	0.90 (0.67-1.22)
Comorbidities (≥1 vs. <1)	1.29 (0.88-1.88)	1.51 (0.90-1.97)	1.15 (0.76-1.76)	1.19 (0.80-1.76)	1.20 (0.81-1.77)
BASDAI (≥4 vs. <4)	0.94 (0.83-1.06)	0.92 (0.84-1.07)	0.97 (0.91-1.03)	0.95 (0.89-1.01)*	0.94 (0.87-1.01)*
C-reactive protein (elevated vs. nonelevated)	1.60 (1.21-2.11)*	1.67 (1.25-2.24)*	1.73 (1.33-2.26)*	1.68 (1.30-2.16)*	1.75 (1.36-2.25)*
Patient Global Assessment (≥23 vs. <23) ^g	1.24 (0.95-1.62)	1.30 (0.97-1.75)	1.32 (1.02-1.72)*	1.28 (1.00-1.64)*	1.24 (0.93-1.59)
NSAID use	0.91 (0.80-1.03)	0.95 (0.86-1.05)	1.00 (0.95-1.06)	0.99 (0.93-1.05)	1.01 (0.93-1.09)
TNFi use	1.00 (0.89-1.13)	0.96 (0.87-1.06)	1.08 (0.99-1.18)	1.06 (0.96-1.17)	1.10 (1.00-1.22)

BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; mSASSS, modified Stoke Ankylosing Spondylitis Spinal Score; NSAID, nonsteroidal anti-inflammatory drug; TNFi, tumor necrosis factor inhibitor.

^a Lateral lumbar bend quartiles: 0-14.5 cm, 14.5-25 cm, 25-34 cm, and >34 cm.

^b Schöber's test quartiles: 0-2 cm, 2-3.5 cm, 3.5-4.5 cm, and >4.5 cm.

^c Occiput-to-wall distance quartiles: >6 cm, 0-6 cm, 0 cm, 0 cm.

^d Lateral cervical bend quartiles: 0-30°, 30-55.5°, 55.5-75°, and >75°.

^e Cervical rotation quartiles: 0-76°, 76-107°, 107-130°, and >130°.

^f Median values used to divide groups.

* P < 0.05.

Longitudinal association of changes in spinal mobility values and mSASSS. Figure 2A–C shows the associations of longitudinal change (difference in spinal mobility compared with the previous visit) of each cervical mobility measure (eg, OTW

distance, cervical rotation, and cervical lateral bending) and in cervical mSASSS values based on multivariable regression models adjusting for baseline mSASSS, study sites, and clinical/demographic variables (Table 3). In the OTW distance analysis, we

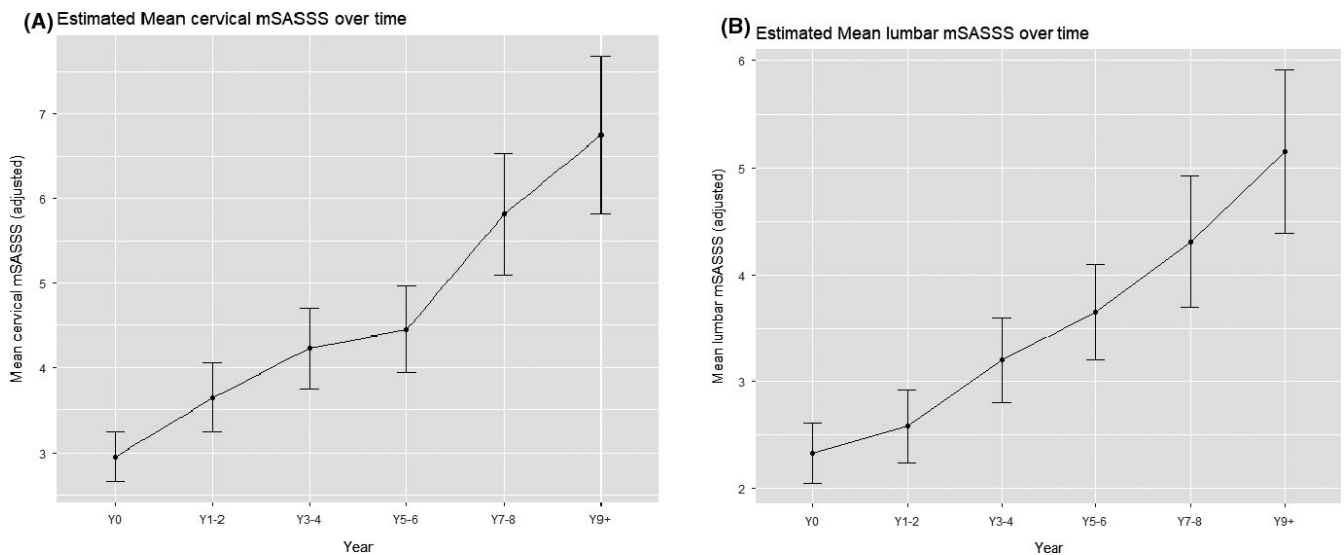
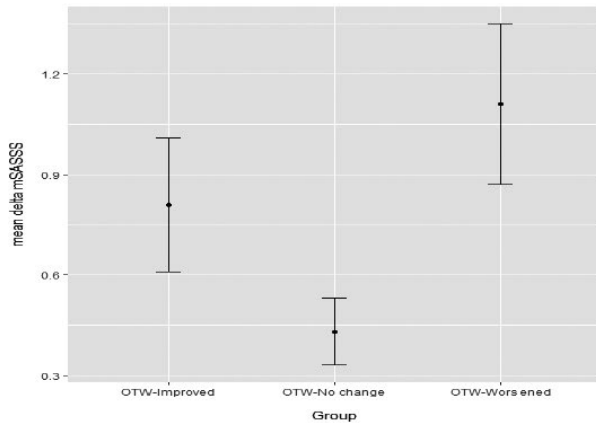
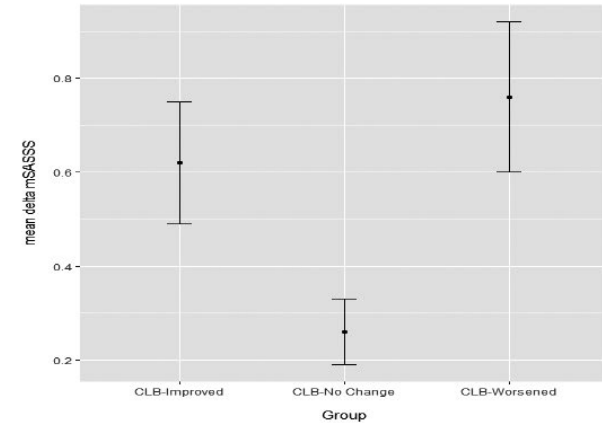


Figure 1. Change in estimated mean cervical (A) and lumbar (B) modified Stoke Ankylosing Spondylitis Spinal Score (mSASSS) over time (years). These figures are from the multivariable modeling accounting for factors, including sex, smoking status, C-reactive protein, and spinal mobility.

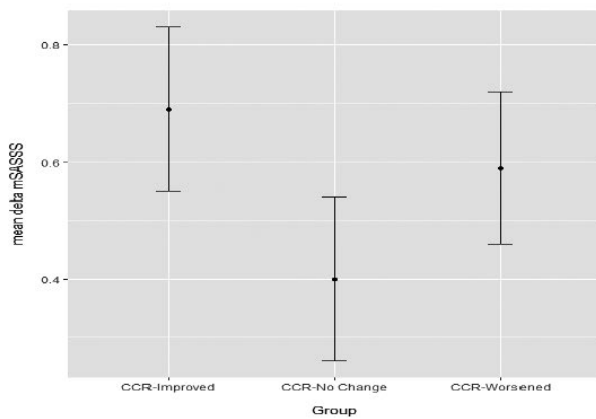
(A) Estimated Mean of Δ mSASSS Cervical by Δ Occiput to wall



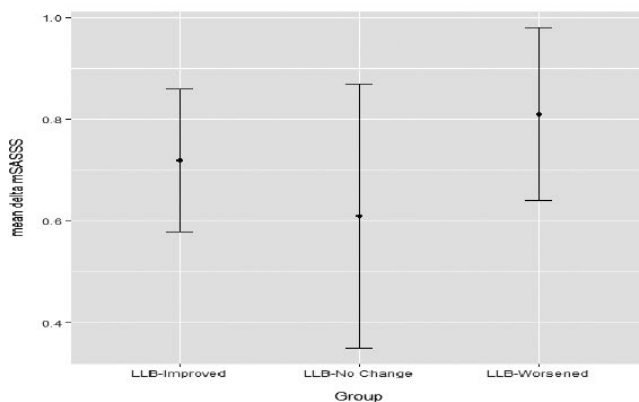
(B) Estimated Mean of Δ mSASSS Cervical by Δ Lateral Cervical bend



(C) Estimated Mean of Δ mSASSS Cervical by Δ Cervical rotation



(D) Estimated Mean of Δ mSASSS Lumbar by Δ Lateral lumbar bend



(E) Estimated Mean of Δ mSASSS Lumbar by Δ Schober

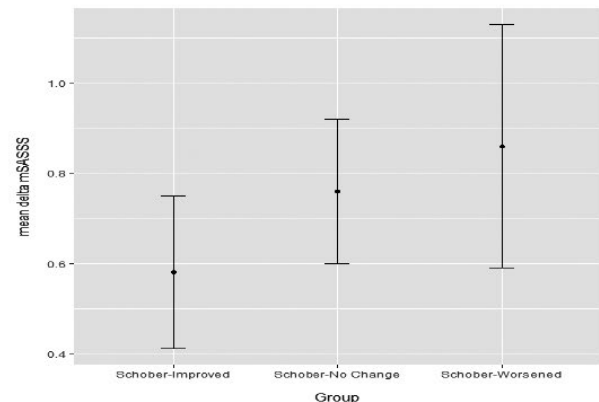


Figure 2. Change in estimated mean modified Stoke Ankylosing Spondylitis Spinal Score (mSASSS) based on change in spinal mobility. We explored the relationship between change in mSASSS and the change in spinal mobility based on the patients' previous clinical visits. **A)** Estimated mean Δ mSASSS cervical by Δ occiput-to-wall (OTW) distance. **B)** Estimated mean Δ mSASSS cervical by Δ lateral cervical bend (CLB). **C)** Estimated mean Δ mSASSS cervical by Δ cervical rotation (CCR). **D)** Estimated mean Δ mSASSS lumbar by Δ lateral lumbar bend (LLB). **E)** Estimated mean Δ mSASSS lumbar by Δ Schöber's test.

observed that both improved and worsened OTW distance was associated with increased change cervical mSASSS compared with no change (Figure 2A). Compared with those whose lateral cervical bending measurements did not change, patients whose measurements worsened or improved also had significant increases

in cervical mSASSS (Figure 2B). No significant differences were observed with cervical mSASSS values and with changes in cervical rotation (Figure 2C). Greater disease duration, higher Patient Global Assessment, and lower BASDAI score were associated with increased mSASSS in the cervical mobility analyses (Table 3).

Table 3. Multivariable analyses of mSASSS and spinal mobility measures over time

Variable	Adjusted Rate Ratio (95% confidence interval)				
	Lateral Lumbar Bend (n = 542)	Schöber's Test (n = 542)	Occiput-to-Wall Distance (n = 518)	Lateral Cervical Bend (n = 518)	Cervical Rotation (n = 518)
Δ Spinal mobility measure					
No change vs. worsened	0.76 (0.34-1.72)	0.92 (0.49-1.72)	0.41 (0.25-0.65)*	0.46 (0.28-0.76)*	0.58 (0.29-1.16)
Improved vs. no change	1.18 (0.53-2.61)	0.94 (0.55-1.62)	1.90 (1.20-3.01)*	2.04 (1.20-3.46)*	1.95 (0.98-3.88)
Improved vs. worsened	0.90 (0.64-1.27)	0.86 (0.58-1.29)	0.78 (0.51-1.19)	0.94 (0.65-1.36)	1.13 (0.80-1.60)
Baseline regional mSASSS	1.01 (1.00-1.03)*	1.01 (1.00-1.03)*	0.99 (0.98-1.01)	1.00 (0.99-1.02)	1.00 (0.99-1.02)
Male vs. female	2.59 (1.58-4.25)*	2.66 (1.62-4.35)*	1.37 (0.74-2.53)	1.65 (0.88-3.07)	1.73 (0.93-3.20)
Disease duration at baseline ≥ 20 vs. < 20	1.02 (1.00-1.04)*	1.02 (1.00-1.04)*	1.02 (1.01-1.04)*	1.02 (1.01-1.04)*	1.02 (1.01-1.03)*
Exercise (≥ 120 min/wk vs. < 120 min/wk) ^a	1.25 (0.83-1.88)	1.27 (0.86-1.91)	1.20 (0.85-1.70)	1.15 (0.67-1.61)	1.12 (0.79-1.57)
Smoking (current vs. other)	1.98 (1.27-3.10)*	2.00 (1.28-3.14)*	1.06 (0.63-1.78)	1.13 (0.66-1.92)	1.09 (0.65-1.84)
Comorbidities (≥ 1 vs. < 1)	1.53 (0.87-2.68)	1.50 (0.88-2.25)	1.21 (0.69-2.12)	1.22 (0.70-2.15)	1.24 (0.70-2.19)
BASDAI (≥ 40 vs. < 40)	0.88 (0.60-1.29)	0.85 (0.59-1.24)	0.44 (0.24-0.70)*	0.45 (0.27-0.77)*	0.46 (0.27-0.77)*
C-reactive protein (elevated vs. nonelevated)	1.60 (1.11-2.30)*	1.57 (1.08-2.29)*	1.38 (0.94-2.03)	1.46 (0.97-2.19)	1.49 (0.99-2.24)
Patient Global Assessment (≥ 23 vs. < 23) ^a	1.23 (0.92-1.62)	1.27 (0.95-1.75)	1.77 (1.12-2.80)*	1.83 (1.19-2.83)*	1.80 (1.14-2.82)*
NSAID use	0.87 (0.56-1.33)	0.90 (0.59-1.38)	1.32 (0.87-1.98)	1.29 (0.84-1.98)	1.26 (0.82-1.93)
TNFi use	1.26 (0.82-1.93)	1.22 (0.81-1.84)	1.27 (0.79-2.03)	1.24 (0.77-1.99)	1.21 (0.75-1.94)

BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; mSASSS, modified Stoke Ankylosing Spondylitis Spinal Score; NSAID, nonsteroidal anti-inflammatory drug; TNFi, tumor necrosis factor inhibitor.

^a Median values used to divide groups.

* $P < 0.05$.

Data summarized in Figure 2D and E show the longitudinal association of lumbar mSASSS values and changes in each of the lumbar spinal mobility measures (lumbar lateral bending and Schöber's test, respectively) with no statistically significant relationships observed. Baseline mSASSS, male sex, disease duration, smoking, and elevated CRP were associated with increased lumbar mSASSS in these lumbar analyses (Table 3).

In our sensitivity analyses, right-censoring regional mSASSS at 32 or less and 34 or less did not result in any significant changes in the associations of changes in mobility with changes in mSASSS, with the exception that baseline regional mSASSS was significantly associated with increased mSASSS in all analyses (supplemental Tables 1 and 2, respectively). When we applied an SDD of 2.5 cm, worsening in OTW distance was significantly associated with a higher cervical mSASSS compared with those patients who had no change (adjusted rate ratio [aRR] = 2.63 [95% CI 1.67-4.34]) or compared with those whose OTW distance actually lessened (aRR = 1.88 [95% CI 1.11-3.22]) (Figure 3A). When we used an SDD of 6.25 cm for lumbar lateral bending, no significant associations with adjusted mSASSS were seen between the change in spinal mobility groupings (improved, no change, and worsened) (Figure 3B). Similarly, applying a SDD of 2.39 cm for Schöber's test did not show a significant association with mSASSS (Figure 3C).

DISCUSSION

Our study showed that, although spinal mobility measures in patients were associated with increased spinal structural disease,

changes in repeated spinal mobility measures were not related to increased radiographic structural progression (as measured by mSASSS) at 2-year intervals. However, in our sensitivity analyses, we did observe that increases in OTW distance may reflect structural progression in cervical mSASSS compared with no change or decreases. This may be explained, in part, because OTW distance, in addition to reflective cervical spinal mobility, reflects structural disease as it captures thoracic kyphosis (25). We also confirmed previous described relationships regarding structural disease in terms of increased mSASSS values with sex, CRP, and disease duration in our multivariable models. Higher BASDAI score was either not associated with or inversely related to greater mSASSS. Current smoking was not statistically significantly associated with increased mSASSS values.

This study adds to our understanding of spinal mobility measures in the context of spinal structural damage/fusion over time. Although earlier studies had suggested that spinal mobility measures could be used as a surrogate for spinal changes demonstrated radiographically after showing group-level correlations between spinal changes and restrictions in range of motion (4), the Wanders et al study demonstrated that the spinal mobility assessment had poor performance characteristics in attempts to discriminate AS spinal changes (5) at a patient level. It has also been described that composite measures, such as the BASMI, remain stable despite increases in structural disease (13). With the use of magnetic resonance imaging (MRI), Machado et al further demonstrated that spinal mobility is also independently determined, in large measure, by spinal inflammation in addition to radiographic damage (10). Our study, however, is the first to

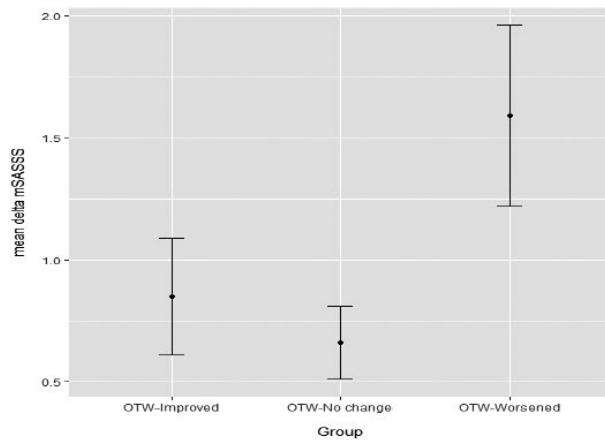
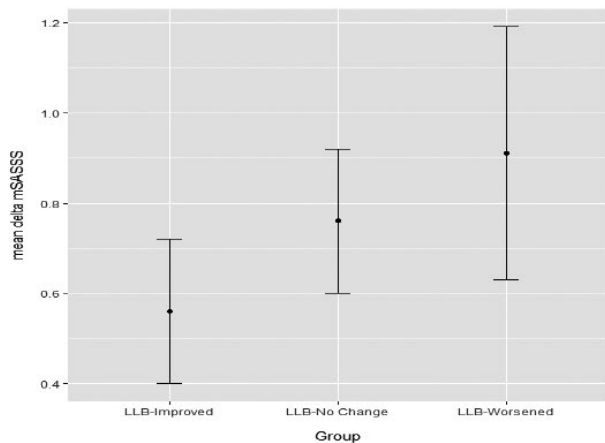
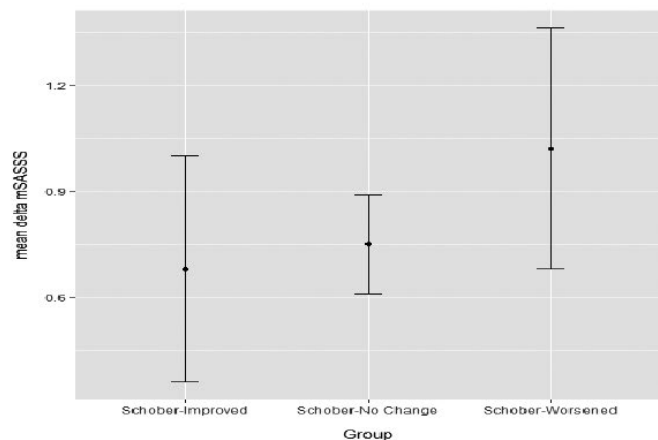
(A) Estimated Mean of Δ mSASSS Cervical by Δ Occiput to wall**(B) Estimated Mean of Δ mSASSS Lumbar by Δ Lateral lumbar bend****(C) Estimated Mean of Δ mSASSS Lumbar by Δ Schober**

Figure 3. Changes in estimated mean modified Stoke Ankylosing Spondylitis Spinal Score (mSASSS) based on changes in spinal mobility with smallest detectable changes applied. **A)** Estimated mean Δ mSASSS cervical by Δ occiput-to-wall (OTW) distance. **B)** Estimated mean Δ mSASSS lumbar by Δ lateral lumbar bend (LLB). **C)** Estimated mean Δ mSASSS lumbar by Δ Schöber's test.

investigate how changes in individual spinal mobility measures relate to local changes in spinal disease, accounting for individual patient effects, over time. Our findings may indicate that, in the assessment of spinal mobility, observed changes in individual patients' mobility measures do not accurately assess structural damage even though poor mobility values do correlate with increased mSASSS values at a group level.

Spinal mobility measures still represent an important spondyloarthritis assessment tool. Observations of abnormalities in spinal mobility raise clinical suspicion and help make the diagnosis of spondyloarthritis (26) despite their lack of specificity. AS spinal mobility measures are sensitive to change (27), with physiotherapy and pharmacotherapy interventions demonstrating improvement (28,29). They are also currently endorsed as an item of the ASAS/OMERACT core sets for assessing AS (2). However, spinal mobility measures have also shown a poor relationship with physical functional measures (30). As the clinical utility of spinal mobility may be more related to spinal inflammation, their

utility may be sublimated by more advanced imaging if serial imaging becomes more used in clinical practice.

This study had both limitations as well as strengths. We used an indirect measurement of spinal inflammation (elevated versus nonelevated CRP levels), which may underrepresent the associations of these values. More direct measures such as MRI have shown a relationship with spinal mobility; however, this tool was not available because of cost limitations. Power to detect differences may have been lost because of the categorical variables that we employed, which, for example, did not detect a consistent association with smoking; continuous variables may have uncovered such an association. The study sites tried to keep the same assessor at all study sites. However, given the multi-year nature of this study, there was turnover of assessors at one study site that may introduce bias into our results. The BASDAI (used in our study) has shown a lesser fit of radiographic disease compared with the AS Disease Activity Score (31). Lastly, although we tried applying the SDDs for our mobility measures,

only three of the five mobility measures have been reported in the literature (23), and they lack consensus in their cutoffs (32). Notable strengths in our study include the very large number of observations we have been able to make over an extended period as well as our accounting for measurement variability by site. We are fortunate to have collected repeated measures in individual patients over time for our analyses as well as to have related these measures to longitudinal health care observations, including disease-specific patient-reported outcomes and medication utilization.

Future directions to fill knowledge gaps about spinal mobility measures should include closer investigation of the relationship between spinal inflammation at the individual spinal level with advanced imaging; these initiatives should further clarify the relationship between spinal mobility, inflammation, and structural progression over time. Additional studies that examine whether spinal mobility or spinal structural disease contribute more to loss of physical functioning may also be an area of future study. Although changes in spinal mobility remain a relevant clinical outcome in clinical trials and care for patients with AS, they may reflect factors other than radiographic structural progression. Furthermore, the addition of future knowledge about minimal detectable change in spinal mobility measures would enhance our ability to appreciate any relationship between spinal mobility and structural damage in the individual patient.

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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 published. Dr. Hwang 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.

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Analysis and interpretation of data. Hwang, Lee, Gensler, Ward, Brown, Rahbar, Ishimori, Weisman, Reveille.

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