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ORIGINAL ARTICLE

Radiologic parameters of ankylosing spondylitis patients treated with anti-TNF-α versus nonsteroidal anti-inflammatory drugs and sulfasalazine

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Abstract

Purpose Limited data are available on the relationship between treatment agents and sagittal balance in ankylosing spondylitis (AS). We investigated radiological features related to treatment agents and compared sagittal balance between patients treated with anti-tumor necrosis factor-α (anti-TNF-α) and those treated with nonsteroidal anti-inflammatory drugs (NSAIDs) and sulfasalazine (SSZ).

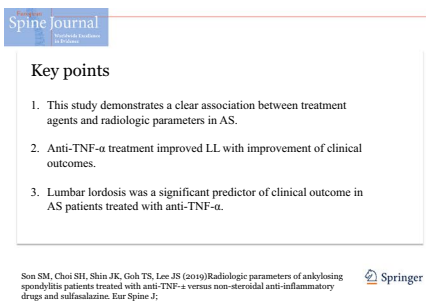
Methods We prospectively enrolled 133 consecutive AS patients. Patients were eligible for the trial if they were under medical treatment with the same treatment agents for at least 1 year. All patients were treated initially with NSAIDs and SSZ. Sixty-nine patients achieved an excellent pain control outcome with these agents (group A). Sixty-four patients who reported of intractable low back pain were switched to anti-TNF-α treatment (group B). Twelve radiographic parameters were measured. Clinical outcome was assessed with the Bath AS Disease Activity Index (BASDAI), erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP). All parameters were measured at enrolment, upon changing treatment agents, and every 6 months during follow-up.

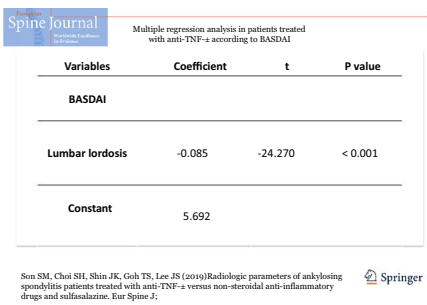
Results The mean ESR, CRP, BASDAI, and thoracic kyphosis at baseline were significantly higher in group B. After treatment, group B had significantly higher lumbar lordosis (LL) and significantly better clinical outcomes. Correlation analysis revealed significant relationships between radiologic parameters and BASDAI. On multiple regression analysis, LL was a significant predictor of BASDAI.

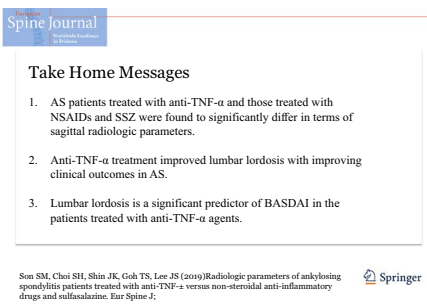
Conclusions This study demonstrated a clear association between treatment agents and radiologic parameters in AS. Anti-TNF-α treatment improved LL with improvement in clinical outcomes. Lumbar lordosis was a significant predictor of clinical outcome in AS patients treated with anti-TNF-α.

Graphical abstract

These slides can be retrieved under Electronic Supplementary Material.







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Keywords Ankylosing spondylitis · Sagittal balance · Radiologic parameters · Anti-TNF-α · Lumbar lordosis

Introduction

Ankylosing spondylitis (AS) is a chronic, inflammatory rheumatic disease characterized by inflammatory back pain due to sacroiliitis and spondylitis, enthesitis, and the formation of syndesmophytes leading to ankyloses [1]. Extraspinal manifestations, including peripheral arthritis, uveitis, and inflammatory bowel disease, are common and contribute to disease morbidity [2]. At advanced stages of the disease, many cases involve spinal deformity such as flattening of the normal lumbar lordosis, which can lead to structural and functional impairments and decreased quality of life [3]. Sagittal balance deteriorates over the course of the disease, producing a rigid thoracolumbar kyphosis. Severe thoracolumbar kyphosis subsequently results in downward tilting of the head and face [4]. The ability of the patient to see above the level of the horizontal gaze progressively worsens, and their center of gravity moves anteriorly, resulting in a stooped, downward-facing posture characteristic of advanced AS [5].

The introduction of anti-tumor necrosis factor-α (anti-TNF-α) has significantly altered the treatment landscape of inflammatory arthritis. It has proven to be an excellent treatment option for reducing AS symptoms [6–8]. The impact of anti-TNF-α on the radiographic progression of AS has been difficult to characterize, in part because of the relatively slow rate of radiographic change in AS and the hurdles it imposes on longer-term placebo-controlled trials. Despite symptomatic improvement, conclusions concerning effect of anti-TNF-α treatment on radiographic progression in patients with AS remain inconsistent [9–12]. Furthermore, while many studies have reported the impact of anti-TNF-α on radiographic progression, limited data are available on the relationship between treatment agents and sagittal balance in AS.

We considered that a more comprehensive understanding of how changes in radiologic parameters relate to the use of different treatment agents and sagittal balance may be useful for the prediction of patients' posture over the course of disease progression and the effects of anti-TNF-α on sagittal balance in AS patients. Therefore, the present study investigated radiological features related to treatment agents and compared sagittal balance between patients treated with anti-TNF-α therapy and those treated with nonsteroidal anti-inflammatory drugs (NSAIDs) and sulfasalazine (SSZ).

Materials and methods

Patient population

One hundred and thirty-three consecutive AS patients were enrolled prospectively at the time of examination between April 2010 and April 2016. AS patients were recruited from patients attending an orthopedic outpatient clinic, and their demographic and clinical characteristics were recorded. The cohort included 33 women and 100 men with a mean age of 42.5 ± 10.9 years. This study was approved by the Clinical Research Ethics Committee of our institution.

All patients who met the most recent modified New York criteria [13] and new Assessment of SpondyloArthritis International Society (ASAS) criteria [14] for AS were considered eligible to participate in the trial if they had been receiving medical treatment with same therapy for at least 1 year. Patients with inflammatory lower back pain were included. However, those with pain originating from the spine owing to other medical condition, such as pregnancy, or pain arising from other parts of the body, such the hips, knees, or shoulders, were excluded. Patients with previous or concurrent diseases of the spine (e.g., spinal deformities like scoliosis, vertebral fracture, spinal stenosis, degenerative intervertebral disk disease, or spinal surgery) or of the lower extremities (e.g., prosthesis, femoral neck or intertrochanteric fracture) were also excluded. Exclusion criteria were age over 60 years and concomitant neurological or psychiatric disease. In addition, patients with complete spinal ankylosis due to bridging syndesmophytes were also excluded because these patients were not expected to demonstrate a difference in spinal mobility after treatment.

All patients were initially treated with NSAIDs and SSZ. Sixty-nine patients demonstrated excellent outcomes for pain control with these agents and continued the therapy (group A). Sixty-four patients complained of intractable low back pain despite treatment for at least 3 months, and their treatment was changed from NSAIDs and SSZ to anti-TNF-α therapy (group B). In these patients, the time at which therapy was changed was regarded as the time of enrolment. No patient was included in both groups simultaneously. The choice of TNF-α inhibitor (infliximab, adalimumab, or golimumab) was based on the judgment of the treating orthopedic surgeon and/or the specific preference of the patient. The standard regimen for infliximab was 5 mg/kg intravenously at 0, 2, and 6 weeks and then every 8 weeks; for adalimumab, 40 mg subcutaneous injection every 2 weeks; and for golimumab, 50 mg subcutaneous injection every 4 weeks.

Radiologic evaluation

Participants underwent lateral whole-spine radiography. Radiographs were taken by 1 technician at a 72-inch standard distance, employing a standard technique and using the same machine in the standing position. All lateral radiographs included both hip joints and cervical vertebrae. To minimize the compensatory mechanism of the lower limb area for sagittal balance, patients were instructed to maintain a neutral position of their lower limbs without knee flexion or ankle extension.

The following radiographic parameters were measured using a picture archiving computer system (PACS Expertise, Marosis, South Korea): sacral slope (SS), pelvic tilt (PT), pelvic incidence (PI), thoracic kyphosis (TK), lumbar lordosis (LL), sagittal vertical axis (SVA), sacrofemoral distance (SFD), ratio of the horizontal distance between the C7 plumb line and posterosuperior corner of the sacrum to SFD (C7/SFD), spinosacral angle (SSA), spinopelvic angle (SPA), cervical lordosis (CL), and cervical sagittal vertical axis (CSVA) (Fig. 1). SS was defined as the angle between the sacral endplate and the horizontal; PT as the angle between the line joining the middle of the sacral endplate

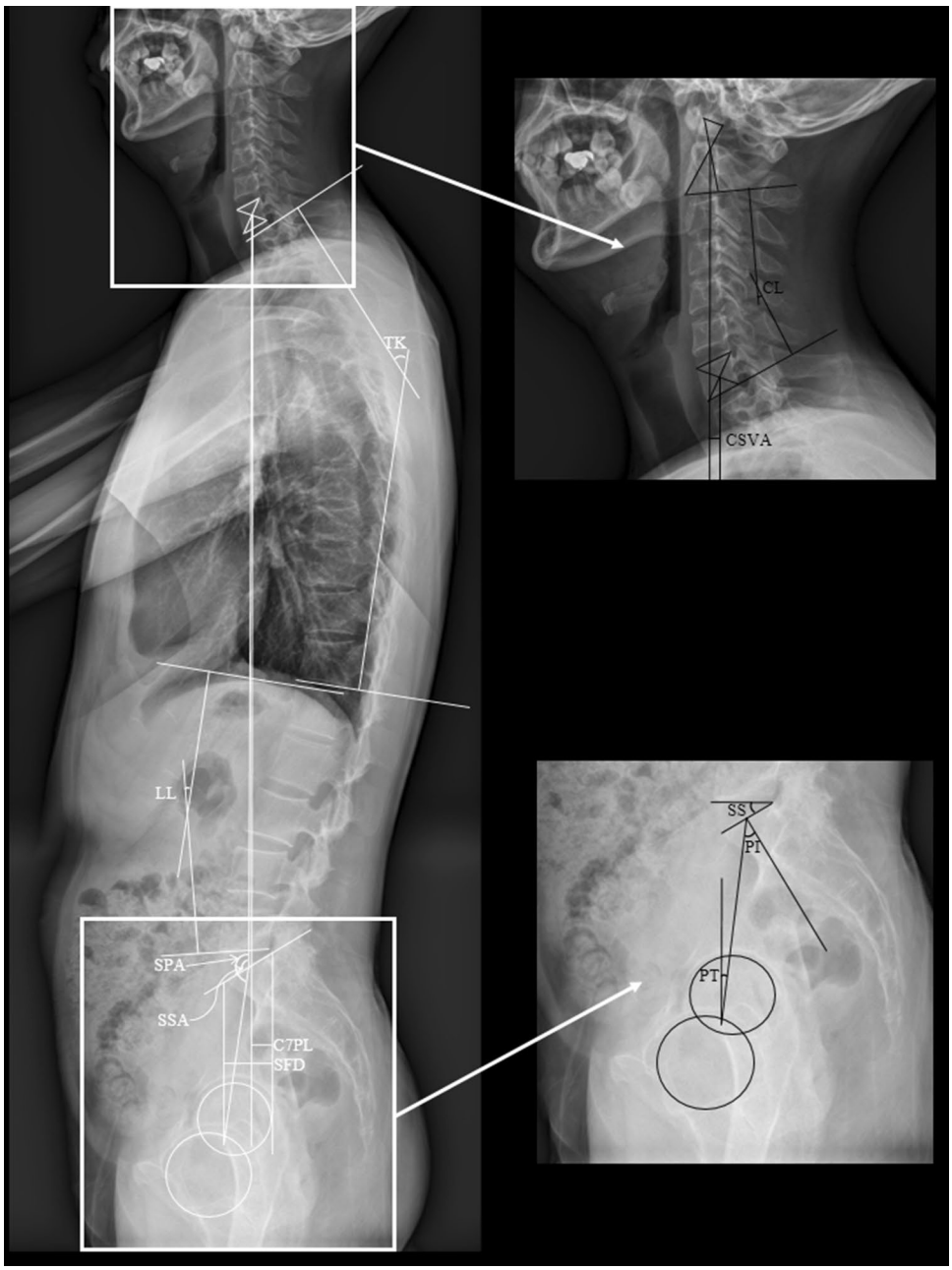

Fig. 1 Measurements of radiologic parameters on an upright whole-spine lateral radiograph

and hip axis and the vertical; and PI as the angle between a line perpendicular to the sacral endplate and a line joining the middle of the sacral plate and the hip axis. TK was measured between the upper endplate of T1 or T2 and the lower endplate of T12 using Cobb's method. LL was measured between the upper endplate of L1 and the upper endplate of S1 using Cobb's method.

Global sagittal balance was measured using C7/SFD ratio, SPA, and SSA. SFD was defined as the horizontal distance between the center of hip rotation and a vertical line passing through the posterior corner of the sacrum. The C7 plumb line was defined as the lateral plumb line from the center of C7. SVA was defined as the horizontal distance between the C7 plumb line and posterosuperior corner of the sacrum. Anterior displacement of the sagittal plumb line was defined as positive. To calculate the C7/SFD ratio, SVA was divided by SFD. The C7/SFD ratio is equal to 0 when the C7 plumb line is on the posterior corner of the sacrum and equal to 1 when the C7 plumb line is on the hip axis. This ratio is negative when the C7 plumb line is posterior to the sacrum and greater than 1 when the C7 plumb line is anterior to the hip axis. According to the classification of global sagittal alignment by Barrey et al., sagittal imbalance was defined by C7/SFD ratio > 0.5 [15]. Eleven patients were in stage of sagittal imbalance in group A and 12 in group B. SSA was defined as the angle between the sacral plate and a line running from the center of C7 to the center of the sacral plate. SPA was defined as the angle between the line drawn from the femoral head center to the sacral plate and a line running from the center of C7 to the center of the sacral plate. CL was measured between the lower endplate of C2 and the lower endplate of C7 using Cobb's method. The C2 sagittal plumb line was defined as the lateral plumb line from the center of C2, considered the point of intersection of crossing diagonals of the C2 vertebral body on a lateral radiograph. CSVA was defined as the distance between the C2 and C7 sagittal plumb lines. All measurements were taken twice independently by three spine surgeons with an interval of 2 weeks between measurements to determine intraobserver (Pearson correlation coefficient = 0.924, range 0.869–0.947) and interobserver errors (Pearson correlation coefficient = 0.897, range 0.864–0.926).

Clinical evaluation

To assess clinical outcome, the Bath AS Disease Activity Index (BASDAI) score was determined, and erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) level were also measured because hematologic factors such as ESR or CRP levels can reflect AS disease activity.

All assessments, including radiography, BASDAI, ESR, and CRP, were performed at enrolment, upon changing treatment agents (this time point was considered the time of enrolment for patients in group B), and every 6 months during the follow-up period.

Statistical analysis

Statistical analysis was performed with SPSS software version 21.0 for Windows (IBM Corp., Armonk, NY, USA). Data were expressed as mean ± standard deviation. A paired *t* test was performed to determine radiological and clinical differences between before and after treatment. A Student's *t*-test was also performed to determine the differences between the two groups. The Mann–Whitney test and Wilcoxon signed-rank test were performed for comparison of sagittal imbalanced patients. Pearson correlation analyses were also performed to determine the relationships between variables. Multiple regression analysis was performed to identify parameters that independently predicted clinical outcome in patients treated with anti-TNF-α. The threshold for statistical significance was P value < 0.05.

Results

Significantly different baseline demographic and disease characteristics were observed between the two groups (Table 1). Group A included 50 men and 19 women with a mean age of 40.8 ± 16.4 years. Group B included 50 men and 14 women with a mean age of 44.4 ± 16.3 years. The follow-up period of group A (608.9 ± 461.1 days) was significantly longer than that of group B (456.3 ± 297.1 days;

Table 1 Baseline characteristics of study patients by treatment group

	Group A (n = 69)	Group B (n = 64)	P value
Sex (M/F) (N)	50/19	50/14	0.454
Age (years)	40.8 ± 16.4	44.4 ± 16.3	0.188
Follow-up (day)	608.9 ± 461.1	456.3 ± 297.1	0.026
TK (°)	43.5 ± 11.1	47.5 ± 11.4	0.043
LL (°)	39.7 ± 14.2	39.5 ± 13.8	0.938
C7PL (mm)	− 1.5 ± 41.4	2.2 ± 37.2	0.597
SFD (mm)	52.8 ± 15.5	47.0 ± 16.6	0.134
C7/SFD	− 0.2 ± 0.9	− 0.1 ± 0.8	0.667
PT (°)	14.5 ± 8.1	15.6 ± 8.5	0.448
SS (°)	35.3 ± 8.2	34.5 ± 8.9	0.563
PI (°)	49.9 ± 10.2	50.1 ± 8.9	0.893
SSA (°)	127.3 ± 9.9	126.7 ± 10.5	0.713
SPA (°)	166.8 ± 11.1	165.9 ± 10.8	0.608
CL (°)	12.3 ± 11.8	11.2 ± 10.5	0.589
CSVA (mm)	13.3 ± 13.5	15.7 ± 17.2	0.378
ESR (mm/h)	14.2 ± 17.7	20.6 ± 15.2	0.027
CRP (mg/dL)	0.6 ± 1.0	1.1 ± 0.9	0.004
BASDAI	6.2 ± 1.2	8.4 ± 0.9	< 0.001

Table 2 Comparison of radiologic, clinical outcomes after treatment by groups

	Group A ($n=69$)	Group B ($n=64$)	P value
TK (°)	45.1 ± 11.4	48.0 ± 10.0	0.121
LL (°)	39.4 ± 14.4	44.7 ± 12.7	0.026
C7PL (mm)	1.4 ± 40.2	− 3.2 ± 41.0	0.513
SFD (mm)	45.0 ± 17.1	47.4 ± 16.4	0.430
C7/SFD	− 0.1 ± 0.9	− 0.3 ± 1.0	0.459
PT (°)	15.1 ± 8.8	16.2 ± 8.6	0.480
SS (°)	34.3 ± 8.3	34.5 ± 9.1	0.887
PI (°)	49.4 ± 10.1	50.7 ± 10.2	0.465
SSA (°)	127.0 ± 8.0	127.7 ± 10.3	0.678
SPA (°)	166.3 ± 11.7	165.9 ± 10.8	0.816
CL (°)	13.2 ± 11.7	12.8 ± 9.1	0.853
CSVA (mm)	13.8 ± 13.4	17.7 ± 17.1	0.149
ESR (mm/h)	13.9 ± 13.2	4.0 ± 2.6	0.013
CRP (mg/dL)	0.8 ± 1.1	0.1 ± 0.1	< 0.001
BASDAI	2.7 ± 1.1	2.3 ± 0.7	< 0.001

$P=0.026$). The mean ESR ($P=0.027$), CRP ($P=0.004$), and BASDAI ($P<0.001$) were significantly higher in group B. Among baseline radiologic parameters, TK was significantly higher in group B (47.5 ± 11.4) than in group A (43.5 ± 11.1; $P=0.043$), whereas the other radiologic parameters did not significantly differ (Table 1).

After treatment, patients in group B (44.7 ± 12.7) had significantly greater lumbar lordosis than did those in group A (39.4 ± 14.4; $P=0.026$). In addition, patients in group B had significantly better clinical outcomes, including ESR (group A: 13.9 ± 13.2, group B: 4.0 ± 2.6, $P=0.013$), CRP (group A: 0.8 ± 1.1, group B: 0.1 ± 0.1, $P<0.001$), and BASDAI (group A: 2.7 ± 1.1, group B: 2.3 ± 0.7, $P<0.001$), than did those in group A. Other radiologic parameters did not significantly differ (Table 2).

On comparing clinical characteristics before and after treatment in each group, there was no significant difference among radiologic parameters in group A. Only BASDAI score (before: 6.2 ± 1.2, after: 2.7 ± 1.1, $P<0.001$) was lower after treatment in group A (Table 3). By contrast, in group B, lumbar lordosis (before: 39.5 ± 13.8, after: 44.7 ± 12.7, $P<0.001$) was significantly increased and ESR (before: 20.6 ± 15.2, after: 4.0 ± 2.6, $P<0.001$), CRP (before: 1.1 ± 0.9, after: 0.1 ± 0.1, $P<0.001$), and BASDAI (before: 8.4 ± 1.0, after: 2.3 ± 0.7, $P<0.001$) were significantly decreased after treatment than those before treatment (Table 4).

In comparison of sagittal imbalanced patients, there was no significant difference in C7/SFD ratio between the groups before and after treatment. Sagittal imbalance was improved after treatment compared with before treatment

Table 3 Comparison between before and after treatment of group A

	Before treatment	After treatment	P value
TK (°)	43.5 ± 11.1	45.1 ± 11.4	0.217
LL (°)	39.7 ± 14.2	39.4 ± 14.4	0.727
C7PL (mm)	− 1.5 ± 41.4	1.4 ± 40.2	0.443
SFD (mm)	42.8 ± 15.5	45.0 ± 17.1	0.060
C7/SFD	− 0.2 ± 0.9	− 0.1 ± 0.9	0.856
PT (°)	14.5 ± 8.1	15.1 ± 8.9	0.205
SS (°)	35.3 ± 8.2	34.3 ± 8.3	0.134
PI (°)	49.9 ± 10.2	49.4 ± 10.1	0.590
SSA (°)	127.3 ± 9.9	127.0 ± 8.0	0.675
SPA (°)	166.8 ± 11.1	166.3 ± 11.7	0.359
CL (°)	12.3 ± 11.8	13.2 ± 11.7	0.442
CSVA (mm)	13.3 ± 13.5	13.8 ± 13.4	0.705
ESR (mm/h)	14.2 ± 17.7	13.9 ± 13.2	0.890
CRP (mg/dL)	0.6 ± 1.0	0.7 ± 1.1	0.228
BASDAI	6.2 ± 1.2	2.7 ± 1.1	< 0.001

Table 4 Comparison between before and after treatment of group B

	Before treatment	After treatment	P value
TK (°)	47.5 ± 11.4	48.0 ± 10.0	0.697
LL (°)	39.5 ± 13.8	44.7 ± 12.7	< 0.001
C7PL (mm)	2.2 ± 37.2	− 3.2 ± 40.9	0.177
SFD (mm)	47.0 ± 16.6	47.4 ± 16.4	0.749
C7/SFD	− 0.1 ± 0.8	− 0.3 ± 1.1	0.094
PT (°)	15.6 ± 8.5	16.2 ± 8.6	0.196
SS (°)	34.5 ± 9.0	34.5 ± 9.1	0.955
PI (°)	50.1 ± 9.7	50.7 ± 10.2	0.350
SSA (°)	126.7 ± 10.5	127.7 ± 10.3	0.236
SPA (°)	165.9 ± 10.8	165.9 ± 10.9	0.991
CL (°)	11.2 ± 10.5	12.9 ± 9.1	0.060
CSVA (mm)	15.7 ± 17.2	17.7 ± 17.1	0.084
ESR (mm/h)	20.6 ± 15.2	4.0 ± 2.6	< 0.001
CRP (mg/dL)	1.1 ± 0.9	0.1 ± 0.1	< 0.001
BASDAI	8.4 ± 1.0	2.3 ± 0.7	< 0.001

Table 5 Comparison of C7/SFD ratio between groups before and after treatment in sagittal imbalanced patients

	Group A	Group B	P value
n (%)	11 (15.94%)	12 (18.75%)	0.672
C7/SFD			
Before treatment	1.38 ± 0.75	1.14 ± 0.45	0.880
After treatment	1.08 ± 0.58	0.84 ± 0.43	0.260
P value	0.248	0.117	

in both groups. However, there was no statistically significant difference (Table 5).

Table 6 summarizes correlations between radiologic parameters in each group. Correlation analysis revealed significant relationships between radiologic parameters and BASDAI (Table 7). In group A, BASDAI correlated with C7/SFD, PT, PI, and SPA. In group B, BASDAI was correlated with TK, LL, SFD, PT, SS, PI, SSA, SPA, and CL.

Multiple regression analysis was performed to identify radiologic parameters that were predictors of clinical outcome after treatment in patients treated with anti-TNF-α revealed lumbar lordosis as a significant predictor of BASDAI (Table 8).

However, in consideration of the degree of overlap in the confidence intervals small absolute clinical difference, and normal measurement error associated with the radiographs being taken, this finding may have been the result of measurement error.

Table 7 Correlations of the radiologic parameters and BASDAI

		BASDAI (group A)	BASDAI (group B)
TK	*r*	0.205	0.566**
LL	*r*	−0.083	−0.513**
C7PL	*r*	0.225	0.007
SFD	*r*	0.222	0.561**
C7/SFD	*r*	0.287*	0.055
PT	*r*	0.342**	0.344**
SS	*r*	−0.057	−0.529**
PI	*r*	0.253*	0.593**
SSA	*r*	−0.117	0.716**
SPA	*r*	−0.286*	0.718*
CL	*r*	−0.019	0.270*
CSVA	*r*	0.156	0.187

*Significant correlation was established at the 0.01 level

**Significant correlation was established at the 0.05 level

Table 6 Correlations (*r*) of the radiologic parameters

	TK	LL	C7Plum	SFD	C7/SFD	PT	SS	PI	SSA	SPA	CL	CSVA
Group A												
TK		0.122	0.034	0.122	0.172	0.095	0.001	0.085	−0.173	−0.089	0.332**	0.334**
LL			−0.363**	0.453**	−0.264*	−0.264*	0.763**	0.397**	0.628**	0.345**	−0.097	−0.163
C7PL				0.542**	0.888**	0.597**	−0.266*	0.305*	−0.533**	−0.816**	0.319**	0.225
SFD					0.483**	0.889**	0.432**	0.424**	−0.489**	−0.828**	0.100	0.271*
C7/SFD						0.492**	−0.170	0.292*	−0.476**	−0.650**	0.355**	0.217
PT							−0.312**	0.621**	−0.416**	−0.914**	0.107	0.295*
SS								0.551**	0.804**	0.307*	−0.006	−0.276*
PI									0.298*	−0.550**	0.088	0.031
SSA										0.520**	0.145	−0.343**
SPA											−0.233	−0.297*
CL												−0.124
CSVA												
Group B												
TK		0.699**	0.007	0.462**	−0.023	0.411**	0.619**	0.699**	0.752**	0.731**	0.310**	0.421**
LL			−0.237	0.286*	−0.249*	0.253*	0.839**	0.774**	0.771**	0.655**	0.156	0.205
C7PL				0.358**	0.874**	0.505**	−0.284*	0.076	−0.214	−0.194	0.306*	0.387**
SFD					0.411**	0.878**	0.178	0.636**	0.417**	0.392**	0.234	0.449**
C7/SFD						0.458**	−0.306*	0.032	−0.214	−0.184	0.222	0.332**
PT							0.129	0.669**	0.321**	0.266*	0.242*	0.502**
SS								0.823**	0.860**	0.740**	0.243*	−0.032
PI									0.828**	0.707**	0.321**	0.263*
SSA										0.971**	0.315**	0.080
SPA											0.328**	0.056
CL												0.009
CSVA												

*Significant correlation was established at the 0.01 level

**Significant correlation was established at the 0.05 level

Table 8 Multiple regression analysis in group B according to BASDAI

Variables	Coefficient	*t*	*P* value
BASDAI			
Lumbar lordosis	−0.085	−24.270	<0.001
Constant	5.692		

Discussion

Although the treatment of spinal deformities associated with AS has become an increasingly important component of many spinal surgery practices, the relevance of radiologic measures in AS remains unclear, although the relationships between radiographic parameters and AS are of evident clinical importance [16]. However, earlier studies reporting radiologic findings in AS did not focus on sagittal balance but rather on spinal radiographic progression [9–12, 17]. Haroon et al. [10] reported that baseline ESR and CRP were significant factors associated with radiographic progression and found a protective effect of anti-TNF-α on radiographic progression in AS. Maas et al. [11] reported that AS patients treated with anti-TNF-α therapy demonstrated slower radiographic progression according to the definitions of Baraliakos et al. [18]. By contrast, several studies reported that anti-TNF-α agents did not prevent the formation of new syndesmophytes and found no improvement in radiological progression after 2–4 years of continuous treatment [12]. To our knowledge, only two previous studies investigated sagittal balance in AS. Shin et al. reported that SVA, SS, and LL were significant parameters in the prediction of clinical outcomes in AS [16]. Lee et al. [19] reported that PT was a significant parameter in the determination of sagittal balance in AS patients and that visual analogue scale was significantly correlated with sagittal spinal parameters.

The sacroiliac joint (SIJ) and the entheses are the most characteristic and sites involved in spondyloarthritis [20, 21]. Inflammation at the interface of the cartilage and bone has been conclusively demonstrated on MRI [21–23] and by immunohistological investigations of SIJ biopsy tissue [24–26]. In cases of early AS, dense mononuclear infiltrates invading the cartilage have been described and TNF-α mRNA has been detected in the inflamed SIJ [27]. Thus, there is evidence for a pathogenic role for TNF-α in AS. Anti-TNF-α is highly effective at suppressing inflammation in AS and functions by suppressing TNF-α and downstream immunological pathways. A previous study reported that there was a significant correlation between the change in TNF-α levels in response to the therapy and clinical improvement. In the study by Zou et al., infliximab downregulated both interferon-ɣ and TNF-α secreted by T cells but did not induce a change in cytokine production by monocytes during 3 months of treatment. This mechanism may be relevant to the clinical efficacy of this therapy [28].

Many studies have demonstrated that anti-TNF-α therapy can improve not only the clinical signs and symptoms of AS but also its associated spinal and sacroiliac inflammation [9, 29–33]. However, limited data have been published on the relationship between treatment agents and radiologic parameters concerning sagittal balance. In the present study, AS patients treated with anti-TNF-α agents (group B) exhibited significantly higher TK and ESR, CRP, and BASDAI at baseline compared to those treated with NSAIDs and SSZ (group A), reflecting relatively higher disease activity. However, although mean TK was increased in both groups, the difference was not statistically significant after treatment. On the contrary, there was no difference in LL between both groups before treatment, but LL was significantly higher in group B than in group A after treatment. In summary, AS patients treated with anti-TNF-α demonstrated no significant difference in the mean TK value and improvement in LL.

On comparing patients of the same group before and after treatment, group A demonstrated no significant differences in radiologic parameters, while lumbar lordosis was improved in group B. Mean BASDAI was decreased in both groups after treatment, but the decrease in group B was significantly greater than that in group A. Correlation analysis revealed that lumbar lordosis was correlated with BASDAI in group B, suggesting that improvement in clinical outcomes may improve LL. In addition, lumbar lordosis was a significant predictor of BASDAI in the patients treated with anti-TNF-α agents on multiple regression analysis.

In general, a reduction in lumbar lordosis can be compensated for by a similar reduction in sacral slope to maintain the relative position of the C7 plumb line [34]. Similarly, an increase in lumbar lordosis can be compensated for by an increase in sacral slope. However, in the present study, although the patients treated with anti-TNF-α agents demonstrated improved lumbar lordosis, sacral slope was not increased significantly. Further evaluation is needed regarding the correlation of these changes.

This study has several limitations that require consideration. First, there was no control group that was comprised of AS patients without any treatment during the follow-up period. However, it is ethically difficult to justify a radiographic study that prospectively incorporates an untreated control group. Second, the follow-up period was relatively short. In AS, spinal radiographic progression is relatively slow and may be detectable only after a minimum of 2 years in some patients [35]. Although AS patients included in this study had received medical treatment for at least 1 year, AS can be heterogeneous in terms of disease activity, deformity, and individuals' ability to compensate for the deformity. However, although it may take years for anti-TNF-α to induce structural changes, we hypothesize that the

improvement in LL was due to clinical improvement, which, as many studies have demonstrated, can occur in a much shorter time frame [6–8, 36]. Third, we prescribed three types of anti-TNF-α agent but did not subdivide patients according to the specific agent. Therefore, we could not detect differences in these agents regarding their effect on sagittal balance. However, several studies have reported that TNF-α inhibitors have similar efficacy in spondyloarthritis [37, 38]. Fourth, we found significant correlations between TK, LL, and BASDAI score in group B, but other radiologic parameters including PT, SS, PI, SSA, SPA, CL, and SFD were also correlated with BASDAI score. Long-term follow-up will be necessary to assess these correlations between clinical and radiological factors in more detail. Fifth, we evaluated clinical outcome using only BASDAI. Other clinical indices such as the Oswestry Disability Index or Scoliosis Research Society questionnaire are needed to evaluate the correlation between radiologic parameters and clinical outcomes more precisely. Finally, as we mentioned previously, there is the possibility of measurement error, as this study relied on radiological measurement.

Despite these limitations, this study is the first to demonstrate a clear association between treatment agents and radiologic parameters in AS. Furthermore, AS patients treated with anti-TNF-α and those treated with NSAIDs and SSZ were found to significantly differ in terms of sagittal radiologic parameters including thoracic kyphosis and lumbar lordosis, and correlation analysis revealed significant relationships between radiologic parameters and clinical outcomes. Anti-TNF-α treatment improved LL with improving clinical outcomes in AS. In addition, LL was a significant predictor of BASDAI in the patients treated with anti-TNF-α agents.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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