Association of adipokines, interleukin-6, and tumor necrosis factor-α concentrations with clinical characteristics and presence of spinal syndesmophytes in patients with ankylosing spondylitis: A cross-sectional study

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Abstract

Objective: To identify correlations of the serum leptin, adiponectin, interleukin-6 (IL-6), and tumor necrosis factor-α (TNF-α) concentrations with the clinical characteristics, presence of spinal syndesmophytes, and body composition in patients with ankylosing spondylitis (AS).

Methods: Forty-eight patients with AS were compared with 41 sex- and age-matched controls. Assessment included clinical characteristics and the presence of spinal syndesmophytes. The serum leptin, adiponectin, TNF-α, and IL-6 concentrations were determined. Body composition was evaluated using dual-energy X-ray absorptiometry.

Results: Patients with AS and controls had similar fat mass and lean mass. Patients with AS had higher serum TNF-α and leptin concentrations than controls (52.3 vs. 1.5 pg/mL and 17.2 vs. 9.0 µg/mL, respectively). The IL-6 and adiponectin concentrations were not significantly different between the two groups. Patients with syndesmophytes had higher leptin concentrations than those without syndesmophytes (22.1 vs. 10.9 µg/mL); this difference remained after adjustment for the body mass index.

Conclusion: Elevated leptin concentrations are associated with spinal radiographic damage in patients with AS and can serve as a biomarker. Future studies should evaluate whether leptin might be a potential target for treatments to avoid structural damage.

Background

Ankylosing spondylitis (AS) is an inflammatory rheumatic disease that mainly affects the axial skeleton, including the sacroiliac joints and spine, and is characterized by chronic low back pain and peripheral joint involvement.[1,2] Syndesmophytes are a distinctive characteristic of AS. They originate from ossification within the spinal joints and ligaments that may lead to bridging of the adjacent vertebral bodies and, in severe cases, progression to bamboo spine.[3,4] Some body composition abnormalities can also be observed in patients with AS. Marcora et al.[5] described a significant decrease in the total lean body mass and appendicular lean mass in patients with AS. Other studies have revealed information about the role of adipose tissue in the production of adipokines and proinflammatory cytokines including tumor necrosis factor-α (TNF-α) and intereukin-6 (IL-6).[6] Leptin and adiponectin are two adipokines that are involved in appetite regulation and play important roles in chronic inflammation.[6,7] Several studies of patients with AS have revealed wide variability in the serum

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leptin and adiponectin concentrations in association with certain disease characteristics.[8–11] Park et al.[8] described a correlation between the serum IL-6 and leptin concentrations. However, few studies have evaluated the relationship between these adipokines and structural spinal damage. Kim et al.[12] reported that the serum leptin concentration is increased in patients with AS who have syndesmophytes. Genre et al.[13] performed a nonsystematic review that emphasized the complex interaction of leptin and adiponectin with proinflammatory cytokines in patients with AS. In this context, whereas leptin induces the production of IL-6 and TNF-α, adiponectin plays a more complex dual role.[13] In two other reports, Miranda-Filloy et al.[14] found no correlation between adipokine concentrations and disease activity or other clinical variables in patients with AS.[15] Many confounders should be taken into account to evaluate the true association between adipokines and clinical variables. Both leptin and adiponectin are strongly influenced not only by the concentrations of proinflammatory cytokines but also by the fat mass and body mass index (BMI). Therefore, measurement of the leptin:BMI ratio is required to accurately assess the leptin concentration in patients with AS. Limited information regarding the correlation of these adipokines with the clinical expression and severity of AS is currently available. Therefore, in the present study, we evaluated the correlations of the serum leptin, adiponectin, IL-6, and TNF-α concentrations with the clinical characteristics, presence of syndesmophytes, and body composition of patients with AS.

Patients and methods

Consecutive patients with AS were recruited from a rheumatology clinic at a secondary-care center in Guadalajara, Mexico (Hospital General Regional 110, IMSS). These patients were selected from a cohort of patients with AS who met the modified 1984 New York criteria for AS[16] and were >18 years of age. We excluded pregnant women and patients with overlapping syndromes (patients with two or more autoimmune rheumatic diseases such as systemic lupus erythematosus, systemic sclerosis, or polymyositis or dermatomyositis),[17] diabetes mellitus, hepatic or thyroid disease, and active infections. Patients were also excluded if they weighed ≥ 100 kg (equivalent to ≥ 220 lb) because of the technical limitations of our dual-energy X-ray absorptiometry (DXA) equipment.

From the same hospital, we enrolled a control group of patients comprising healthy blood donors matched by sex, age, and BMI. The control patients had no family history of connective tissue disease.

Clinical assessment

Both groups were assessed with a structured interview regarding their clinical characteristics and history of comorbidities. The BMI was calculated as the body weight in kilograms divided by the square of the patient's height in meters (kg/m^2). Assessment of patients with AS included the following: evaluation of peripheral arthritis and enthesitis, disease activity according to the results of the Bath Ankylosing Spondylitis Diseases Activity Index (BASDAI),[18] and function according to the results of the Bath Ankylosing Spondylitis Functional Index (BASFI).[19] We also assessed the physician's and patients' global assessment of disease activity using a visual analog scale ranging from 0 to 100 mm.

Radiologic assessment

All patients with AS were evaluated with anteroposterior and lateral X-rays of the cervical and lumbar spine to assess the presence of syndesmophytes. Syndesmophytes were defined as bony protuberances

associated with ossification of the spinal ligaments without involvement of the inter-vertebral discs.[20] Patients with AS were further classified into two subgroups according to their radiographic spine findings: patients with and without syndesmophytes.

Leptin and adiponectin concentrations

On the same day of the interview, fasting blood samples were collected and immediately centrifuged, and the serum was stored at −20°C for a maximum of 4 months. The serum adiponectin and leptin concentrations were measured by enzyme-linked immuno-sorbent assay (ELISA) using commercial kits (IBL International, Hamburg, Germany). According to the manufacturer, the detection range for leptin was 1.0 to 100 ng/mL and the assay sensitivity was 1 ng/mL, and those for adiponectin were 26 to 100 ng/mL and 26 ng/mL, respectively.

TNF-α and IL-6 concentrations

The serum TNF-α and IL-6 concentrations were measured by ELISA using commercial kits (R&D Systems, Minneapolis, MN, USA). According to the manufacturer, the detection range for TNF-α was 15.6 to 1000 pg/mL and the assay sensitivity was <5.5 pg/mL, while those for IL-6 were 3.12 to 300 pg/mL and <7.0 pg/mL, respectively.

All laboratory measurements were carried out by independent researchers who were blinded to the clinical characteristics of the patients who provided the serum samples. The serum cytokine and adipokine concentrations were measured using the same sample.

Body composition

A total body scan was performed using a *LUNAR Prodigy 2000 Densitometer (GE Medical Systems Lunar, Madison, WI. USA)*. Body composition measurements were obtained from a total body scan, and the lean mass and fat mass in grams were determined. All patients were scanned while wearing light clothing and lying in the supine position. DXA differentiates the tissue attenuation of photons. It discriminates two substances in a given system and provides soft tissue measurements from which the percentage of body fat and fat-free mass are computed. From these data, estimates of the total body bone mineral content are obtained.[21]

Statistical analysis

Quantitative variables are expressed as mean ± standard deviation, and qualitative variables are expressed as frequency and percentage. For independent samples, Student's t-test was used to compare the serum concentrations of adipokines, cytokines, and other quantitative variables between patients with AS and controls. Similarly, unpaired Student's t-test was used to compare these concentrations between patients with AS with and without syndesmophytes. The chi-square test (or Fisher's exact test if required) was used to compare proportions between these groups. Pearson's correlation test (r) was performed to assess the strength of association among quantitative variables. All statistical tests were two-sided, and the P value for significance was set at 0.05. Statistical analyses were performed with SPSS ver. 23.0 statistical software (IBM Corp., Armonk, NY, USA).

Ethics

The present study was approved by the Research and Ethics Committee of the hospital (CLIEIS 1301) and included two components of the research line (approval numbers (2008-1301-47 and 2009-1301-96). All participants provided written informed consent before enrollment. This study was performed according to the principles of the Declaration of Helsinki.

Results

General characteristics of patients with AS

Table 1 shows the general characteristics of the patients with AS. The patients had a mean disease duration of 9.4 years, a mean patient global assessment of disease activity score of 5.31, a mean BASDAI score of 5.22, and a mean BASFI score of 4.24. The percentages of drugs used for treatment were as follows: disease-controlling anti-rheumatic therapy, 94%; anti-TNF drugs, 29%; and corticosteroids, 15%.

Table 1. Characteristics of patients with ankylosing spondylitis.

Features	Patients (n = 48)
Male sex	30 (63)
Disease duration (years)	9.4 ± 7.3
Disease activity, patient (VAS)	5.3 ± 3.0
Disease activity, physician (VAS)	4.1 ± 3.0
BASDAI score	5.2 ± 2.4
BASFI score	4.2 ± 2.6
Occiput-to-wall distance (cm)	3.2 ± 5.5
Tragus-to-wall distance (cm)	13.5 ± 5.4
Chest expansion	3.7 ± 1.5
Finger-to-floor distance (cm)	23.7 ± 17.2
Inter-malleolar distance (cm)	80.3 ± 28.1
Lumbar flexion (Schober test) (cm)	3.8 ± 1.9
Treatment	
DC-ART synthetics	45 (94)
Sulfasalazine	29 (60)
Methotrexate	28 (58)
Others	17 (35)
Anti-TNF agents	14 (29)
Etanercept	8 (17)
Infliximab	6 (13)
Adalimumab	1 (2)
Glucocorticoids	7 (15)

Data are presented as n (%) or mean ± standard deviation. VAS: visual analog scale, BASDAI: Bath Ankylosing Spondylitis Disease Activity Index, BASFI: Bath Ankylosing Spondylitis Functional Index, DC-ART: disease-controlling antirheumatic therapy, TNF: tumor necrosis factor

Comparison of patients with AS and controls

Table 2 compares the serum leptin, adiponectin, TNF-α, and IL-6 concentrations between the patients with AS ($n = 48$) and controls ($n = 41$). There were no significant differences in the following variables that could have affected adipokine levels between the patients and controls: age (44.3 vs. 46.2 years, respectively), BMI (26.9 vs. 27.5 kg/m^2, respectively), fat mass (25.5 vs. 25.2 g, respectively), and lean mass (43.9 vs. 47.5 g, respectively). With respect to adipokines, patients with AS had significantly higher serum leptin concentrations than did controls (17.2 ± 16.4 vs. 9.0 ± 7.1 μg/mL, respectively; $P = 0.05$). The adiponectin concentration was not significantly different between patients and controls (9.1 ± 4.1 vs. 9.6 ± 4.7 μg/mL, respectively). With respect to cytokines, the serum TNF-α concentration was significantly higher in patients than controls (52.3 ± 140.6 vs. 1.5 ± 8.3 pg/mL, respectively; $P = 0.01$), whereas no difference was observed in the IL-6 concentration (4.2 ± 9.0 vs. 1.6 ± 3.3 pg/mL, respectively).

Association of cytokines, adipokines, and other disease characteristics with the presence of syndesmophytes

Table 3 compares the clinical characteristics and serum concentrations of adipokines and cytokines between patients with AS with and without syndesmophytes. Patients with syndesmophytes were older (44.3 vs. 36.7 years, respectively; $P < 0.001$). The serum leptin concentration was higher in patients with than without syndesmophytes (22.1 vs. 10.9 μg/mL, respectively; $P = 0.01$); this difference remained even after adjustment for BMI (0.76 vs. 0.41 μg/mL, respectively; $P = 0.009$). We observed no significant difference in the serum adiponectin, TNF-α, or IL-6 concentration between patients with and without syndesmophytes.

Table 2. Comparison of clinical characteristics, adipokines, and cytokines between patients and controls.

Features	Patients (n = 48)	Controls (n = 41)	p
Male sex	30 (63)	27 (66)	0.74
Salaried employment	23 (48)	34 (83)	0.001
Age (years)	44.3 ± 11.4	46.2 ± 10.7	0.44
Height (cm)	164.6 ± 8.9	166.4 ± 10.0	0.36
Weight (kg)	73.9 ± 13.0	75.8 ± 13.5	0.50
BMI (kg/m^2)	26.9 ± 4.4	27.5 ± 4.3	0.53
Fat mass (g)	25.5 ± 8.0	25.2 ± 8.5	0.86
Lean mass (g)	43.9 ± 8.8	47.5 ± 12.3	0.11
Leptin (μg/mL)	17.2 ± 6.4	9.0 ± 7.1	0.05
Adiponectin (μg/mL)	9.1 ± 4.1	9.3 ± 4.7	0.77
TNF-α (pg/mL)	52.3 ± 140.6	1.5 ± 8.3	0.01
IL-6 (pg/mL)	4.2 ± 9.0	1.6 ± 3.3	0.08

Data are presented as n (%) or mean ± standard deviation. BMI: body mass index, TNF-α: tumor necrosis factor-α, IL-6: interleukin-6. Proportions were compared with the chi-square test. Means were compared with the unpaired Student's t-test.

Table 3. Comparisons between patients with ankylosing spondylitis with and without syndesmophytes.

Features	With syndesmophytes (n = 27)	Without syndesmophytes (n = 21)	p
Male sex	14 (51.9)	16 (76.2)	0.13
Age (years)	44.3 ± 11.4	36.7 ± 10.5	<0.001
Disease duration (years)	10.2 ± 8.1	8.3 ± 6.3	0.37
BMI (kg/m^2)	27.83 ± 4.37	25.66 ± 4.11	0.08
Fat mass (g)	27.8 ± 7.4	22.8 ± 7.4	0.03
BASDAI score	5.2 ± 2.4	5.2 ± 2.5	0.98
BASFI score	4.3 ± 2.8	4.2 ± 2.6	0.95
Finger-to-floor distance (cm)	28.2 ± 17.5	17.8 ± 15.2	0.03
Intermalleolar distance (cm)	73.3 ± 25.3	89.2 ± 29.5	0.05
Lumbar flexion (Schober test) (cm)	3.2 ± 2.0	4.5 ± 1.7	0.02
Leptin (μg/mL)	22.1 ± 19.8	10.9 ± 6.9	0.01
Leptin:BMI ratio	0.76 ± 0.6	0.41 ± 0.2	0.009
Adiponectin (μg/mL)	9.0 ± 4.8	9.1 ± 3.1	0.93
TNF-α (pg/mL)	68.2 ± 177.1	31.8 ± 70.0	0.38
IL-6 (pg/mL)	5.6 ± 11.4	4.0 ± 5.8	0.60

Data are presented as n (%) or mean ± standard deviation. BMI: body mass index, BASDAI: Bath Ankylosing Spondylitis Disease Activity Index, BASFI: Bath Ankylosing Spondylitis Functional Index, TNF-α: tumor necrosis factor-α, IL-6: interleukin-6. Proportions were compared with the chi-square test. Means were compared with the unpaired Student's t-test.

Correlation of cytokine and adipokine concentrations with selected clinical characteristics of patients with AS

Table 4 shows the results of the correlation analysis of adipokines, cytokines, and body composition with clinical characteristics in the 48 patients with AS. As expected, leptin was positively correlated with the BMI ($r = 0.57$, $P < 0.001$) and fat mass ($r = 0.61$, $P < 0.001$). Adiponectin exhibited a negative correlation with weight ($r = -0.31$, $P = 0.02$), BMI ($r = -0.31$, $P = 0.02$), and fat mass ($r = -0.29$, $P = 0.04$). TNF-α was correlated with lean mass ($r = 0.28$, $P = 0.04$), but IL-6 was not correlated with any of the evaluated variables.

Both leptin and the leptin:BMI ratio were negatively correlated with the intermalleolar distance ($r = -0.33$, $P = 0.01$).

Adiponectin showed a negative correlation with the tragus-to-wall distance ($r = -0.29$, $P = 0.04$). TNF-α was positively correlated with the occiput-to-wall distance ($r = 0.48$, $P = 0.001$) and tragus-to-wall distance ($r = 0.52$, $P = 0.001$) and negatively correlated with lumbar flexion according to the Schober test ($r = -0.28$, $P = 0.05$).

A correlation analysis was performed (with data not shown in tables) between the serum adipokine and cytokine concentrations, and no correlations were observed between the serum leptin and adiponectin concentrations. We also observed no correlation between leptin and TNF-α ($r = -0.17$, $P = 0.23$) and IL-6 ($r = -0.49$, $P = 0.74$). Similar results were observed between adiponectin and TNF-α ($r = -0.23$, $P = 0.10$) and IL-6 ($r = -0.05$, $P = 0.72$).

Table 4. Correlation of adipokines and cytokines with clinical features of ankylosing spondylitis.

	Leptin		Leptin:BMI		Adiponectin		TNF-α		IL-6	
	r	p	r	p	r	p	r	p	r	p
Anthropometric characteristics										
Weight (kg)	0.21	0.14	0.11	0.42	−0.31*	0.02	0.26	0.69	−0.14	0.33
Height (cm)	−0.41**	0.03	−0.41	0.003	0.07	0.96	0.18	0.20	−0.24	0.09
BMI (kg/m^2)	0.57**	<0.001	–	–	−0.31*	0.02	0.17	0.22	0.01	0.90
Fat mass (%)	0.61**	<0.001	0.52	<0.001	−0.29*	0.04	0.06	0.66	−0.02	0.86
Lean mass (%)	−0.25	0.07	−0.31	0.03	−0.21	0.14	0.28*	0.04	−0.17	0.07
Disease characteristics										
Disease duration (years)	−0.36	0.80	−0.02	0.85	0.19	0.18	0.22	0.12	−0.04	0.78
Disease activity by patient (years)	−0.54	0.71	−0.04	0.78	0.21	0.14	0.15	0.28	0.17	0.22
Disease activity by physician	−0.01	0.91	0.01	0.95	0.07	0.61	0.15	0.30	0.26	0.71
Morning stiffness	−0.33	0.82	0.01	0.97	0.17	0.23	0.09	0.53	0.16	0.26
BASDAI score	0.32	0.83	0.05	0.74	0.53	0.72	−0.21	0.88	0.10	0.48
BASFI score	0.001	1.00	−0.003	0.10	−0.32	0.83	−0.35	0.81	0.08	0.58
Occiput-to-wall distance	−0.09	0.53	−0.09	0.53	−0.21	0.14	0.48**	<0.001	−0.12	0.93
Tragus-to-wall distance	−0.31	0.83	−0.02	0.84	−0.29	0.04	0.52**	<0.001	−0.00	0.99
Chest expansion	−0.07	0.59	−0.18	0.90	0.07	0.59	−0.05	0.69	0.06	0.64
Finger-to-floor distance	0.06	0.66	0.07	0.61	−0.22	0.13	0.26	0.06	0.19	0.19
Intermalleolar distance	−0.33*	0.01	−0.30	0.01	0.06	0.64	0.38	0.79	−0.35	0.81
Lumbar flexion (Shober test)	−0.001	0.99	−0.02	0.87	0.04	0.74	−0.28	0.05	−0.18	0.19

BMI: body mass Index, BASDAI: Bath Ankylosing Spondylitis Disease Activity Index, BASFI: Bath Ankylosing Spondylitis Functional Index, TNF-α: tumor necrosis factor-α, IL-6: interleukin-6

Discussion

The present study revealed a significantly higher serum leptin concentration in patients with AS than controls despite a similar BMI between the two groups, whereas patients with AS plus syndesmophytes had a higher serum leptin concentration than both patients without syndesmophytes and controls. This higher leptin concentration in patients with AS was correlated with a shorter intermalleolar distance, whereas no correlation was observed between the leptin concentration and disease activity. On the other hand, a higher TNF-α concentration was correlated with more limited spinal mobility, although no correlations were identified between the serum adiponectin or IL-6 concentration and any clinical variables evaluated in these patients.

Different studies of nonrheumatic populations have demonstrated that an increase in BMI is closely associated with a high leptin concentration and inversely associated with a low adiponectin concentration[22,23] In the patients with AS in the present study, a higher BMI and fat mass were associated with a higher leptin concentration and lower adiponectin concentration, similar to the data described for the general population.[22] We also observed that although the BMI was similar between patients with AS and controls, the serum leptin concentration was around two-fold higher in patients with AS, signifying that this increase in leptin may be influenced by AS-related factors. Previous studies comparing the leptin concentration between patients with AS and controls have revealed some discrepancies.[8,10,11,14] A study performed by Toussirot et al.[11] showed lower leptin concentrations in patients with AS than in controls, although their study only included men with active disease. In contrast, we included both men and women as well as patients with active and inactive disease in the present study. Derdemezis et al.[10] and Miranda-Filloy et al.[14] found no

differences in the serum leptin concentration between patients with AS and controls, although these authors included only men with active AS undergoing treatment with infliximab. In contrast, Park et al.[8] found higher leptin concentrations in patients with AS than in controls. Kim et al.[12] initially observed no differences in the leptin concentration between patients with AS and controls, but differences appeared when they analyzed the patients according to the presence of syndesmophytes; higher serum leptin concentrations were found in this subgroup.

Whereas the leptin concentration was higher in patients with AS than controls, the adiponectin concentration was similar between the two groups, suggesting that this adipokine dos not play a relevant role in AS. Derdemezis et al.[10] and Toussirot et al.[11] analyzed the adiponectin concentration in patients with AS. While Toussirot et al.[11] did not observe a difference in the adiponectin concentration between patients with AS and controls, Derdemezis et al.[10] observed a higher adiponectin concentration in patients with AS.

Some independent studies evaluating the relationship between adipokines and the clinical features of AS revealed no correlation between adipokines and disease activity.[8,10,11,15,24,25] This finding is similar to that obtained in our study. Park et al.[8] observed that the serum leptin concentration may be correlated with the BASDAI score and a high C-reactive protein concentration. Various confounders may explain the differences between the findings obtained by Park et al.[8] and those revealed in other studies; for example, Park et al.[8] included only men with a recent diagnosis, whereas our study included both men and women with a longer disease duration, signifying that the concentrations of these adipokines may change during disease evolution.

Leptin is considered to promote inflammation by inducing Th1 cell development.[26] Leptin stimulates CD4 T-lymphocyte proliferation, regulates macrophage phagocytosis,

and increases the production of IL-6, IL-12, and TNF-α.[27,28] Adiponectin is also considered to have anti-inflammatory properties because it induces IL-10[29] and decreases the production of TNF-α; however, TNF-α might also downregulate adiponectin production.[30] Our results of a significant association between severe spinal damage in AS manifested by the presence of syndesmophytes and high TNF-α concentrations is in accordance with the role of this cytokine in inflammation of the spine and sacroiliac joints.[31]

We found no correlations between the IL-6 concentration and the BMI, fat mass, or disease activity. In contrast, Park et al.[8] reported that the serum IL-6 concentration was correlated with the serum leptin concentration and the disease activity in their patients with AS. The role of IL-6 in AS remains controversial; Gratacos et al.[32] and Tutuncu et al.[33] found that the serum IL-6 concentration was higher in patients with AS than controls. However, although we only observed a trend toward higher IL-6 concentrations in patients with AS, this trend did not reach statistical significance. More recently, Syrbe et al.[25] evaluated the relationship between serum adipokines concentrations and radiographic spinal progression after 2 years. These authors found that the visfatin concentration was associated with radiographic progression, whereas no relationship was observed between the baseline adiponectin or resistin concentration and radiographic damage. However, the authors did not evaluate leptin. In the present study, leptin was associated with the presence of syndesmophytes. In a recent meta-analysis, Mei et al.[34] observed no significant differences between the plasma or serum leptin concentration between patients with AS and controls. Instead, we observed significantly higher leptin concentrations in patients with AS than in controls. An important factor to consider when analyzing these differences is the influence of confounders that modify the serum leptin concentration; some of these confounders were not entirely adjusted for in the meta-analysis by Mei et al. [34] In the present study, the patients' BMI, sex, age, and fat mass, all of which modify the serum leptin concentration, were very similar between patients with AS and controls; therefore, we minimized the influence of these confounders on the serum concentration of this adipokine. Toussirot et al.[35] found that among patients with AS, the serum leptin concentration and leptin:body fat mass ratio were lower in men than women. Kim et al.[12] found that patients with syndesmophytes had a higher serum leptin;BMI ratio, which supports our finding that a higher serum leptin concentration and high leptin:BMI ratio are associated with syndesmophytes. However, we also performed a more extensive assessment of other potential biomarkers, including TNF-α, IL-6, and adiponectin, and observed that these other molecules had no association with syndesmophytes. Genre et al.[13] performed a review of several studies evaluating changes in leptin[14] and adiponectin[15] in patients with AS undergoing treatment with anti-TNF agents; the majority of these studies involved Spaniard patients. Interestingly, similar findings regarding the leptin or adiponectin concentration are observed between patients with AS and patients with other diseases such as rheumatoid arthritis and psoriasis.[36–39]

Some limitations of our study must be considered. First, the cross-sectional design allowed for only a snapshot in time of the characteristics in a single group of patients, whereas the influence of adipokines and cytokines is complex and may vary at different disease stages. A cohort study evaluating changes in the serum concentrations of these adipokines may determine whether leptin contributes to the inflammation observed in these patients.

Conclusions

An elevated leptin concentration is associated with spinal radiographic damage in

patients with AS and can serve as biomarker for spinal syndesmophytes. Future studies should be performed to evaluate whether leptin might be a potential target for treatments to avoid structural damage.

Declaration of conflicting interest

The authors declare that there is no conflict of interest.

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