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Adipose tissue, serum adipokines, and ghrelin in patients with ankylosing spondylitis

Éric Toussirot[a,b,*], Gérald Streit[a], Nhu Uyen Nguyen[c], Gilles Dumoulin[c], Gaëlle Le Huédé[a], Philippe Saas[d], Daniel Wendling[a]

[a]*Department of Rheumatology, University hospital Jean Minjoz, Bd Fleming, F-25030 Besançon, Cédex, France*
[b]*CIC-biotherapy (CIC-B), St Jacques Hospital, F-25030 Besançon, France*
[c]*Department of Physiology, University hospital Jean Minjoz, Bd Fleming, F-25030 Besançon, Cédex, France*
[d]*INSERM U645, University of Franche-Comté, EFS Bourgogne Franche-Comté-Plateforme de BioMonitoring, IFR 133, Bd Fleming, F-25020 Besançon, France*

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Abstract

Adipokines such as leptin and adiponectin are involved in the regulation of inflammation. Ghrelin, a gastric peptide playing a role in the appetite regulation, possesses anti-inflammatory properties. In this study, we evaluated the circulating levels of adipokines (leptin as potential proinflammatory and adiponectin as anti-inflammatory marker) and ghrelin and the fat mass in patients with ankylosing spondylitis (AS). Serum leptin, adiponectin, and ghrelin were evaluated in 53 AS patients with active disease (mean Bath Ankylosing Spondylitis Disease Activity Index >40) and 35 controls. Fat and lean masses were determined using dual-energy x-ray absorptiometry. Fat and lean masses did not differ between patients and controls. Ankylosing spondylitis patients had lower leptin levels compared with controls, even after adjustment for fat mass (AS vs controls: leptin, 7.6 ± 1.3 ng/mL vs 10.3 ± 1.5 ng/mL; leptin [in nanograms per milliliter]/fat mass [in kilograms], 0.28 ± 0.04 vs 0.44 ± 0.04; $P = .006$ and $P = .0003$, respectively). Serum adiponectin did not differ between patients and controls, whereas circulating ghrelin was higher in AS patients (1354.6 ± 70.5 pg/mL vs 1008.0 ± 82.5 pg/mL; $P = .001$). However, all these results were significant only for male patients. No correlation was found between leptin and adiponectin, and erythrocyte sedimentation rate, C-reactive protein levels, tumor necrosis factor α, or Bath Ankylosing Spondylitis Disease Activity Index. Ankylosing spondylitis patients had no changes in fat mass. Leptin production was reduced in contrast with normal levels of adiponectin. These adipokine results, together with high serum ghrelin levels, may influence the inflammatory response in AS.

1. Introduction

Ankylosing spondylitis (AS) is a chronic inflammatory disease that mainly affects the axial skeleton. Weight loss is observed during acute and chronic inflammatory processes and may influence physical activity, quality of life, and also survival. Indeed, changes in body composition and particularly lean mass have been described in rheumatic diseases, mainly rheumatoid arthritis (RA) [1] and systemic lupus erythematosus [2]. These changes were related to increased levels of pro-inflammatory cytokines such as tumor necrosis factor (TNF) α, interleukin (IL) 1, or IL-6 [1].

Inflammatory cytokines are produced by different cell subtypes, circulating monocytes, or lymphocytes, but can also have other cellular sources such as macrophages from fat tissue. Indeed, adipose tissue is no longer considered as an inert tissue devoted to energy storage, but is also an active participant regulating physiologic and pathologic processes including immunity and inflammation [3,4]. Besides the production of classic cytokines, fat tissue, and notably adipocytes, produced and released itself certain proteins or adipokines [4]. Leptin and adiponectin are 2 of these adipokines, and their biological functions have been well characterized [5,6]. Indeed, leptin has a wide range of biological properties including the regulation of food intake, energy expenditure, and also immunity. Leptin is rather considered as a proinflammatory molecule linking fat tissue to the cells participating in the inflammatory

* Corresponding author.
E-mail address: etoussirot@chu-besancon.fr (É. Toussirot).

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response [5,7]. Conversely, leptin may also possess anti-inflammatory properties [8]. Adiponectin is best known for its role in the regulation of insulin sensitivity and acts as an insulin-sensitizing hormone with reduced blood concentration in obesity, metabolic syndrome, and type 2 diabetes mellitus. On the other hand, adiponectin is considered as an anti-inflammatory molecule by reducing the activity and the production of cytokines such as TNF-α [5,9]. In addition, leptin and adiponectin have been implicated in experimental models of inflammation and in human diseases such as RA, multiple sclerosis, or asthma [5].

Ghrelin is a recently described growth hormone (GH)–releasing molecule produced by the stomach. It induces a positive energy balance by stimulating appetite. It also has antagonist effects on leptin through hypothalamic pathway and thus has potential influences in the regulation of weight. In addition, interaction between ghrelin and immune cells has recently been described [10].

Thus, adipose tissue must be currently considered as an active tissue producing molecules involved in the control of appetite and also in the regulation of inflammatory responses. In this study, we aimed at evaluating adipose tissue in patients with AS to examine the contribution of fat-derived molecules to the inflammatory response. Thus, circulating levels of leptin, adiponectin, and also ghrelin were evaluated; and we examined the relationships between these molecules and disease activity. Anabolic hormones such as GH and insulin growth hormone I (IGF-I) were assessed because of their interrelations with leptin, ghrelin, and body composition [11].

2. Materials, patients, and methods

2.1. Subjects

2.1.1. Patients

Fifty-three white outpatients consecutively seen in our department were included. They all responded to the modified New York criteria [12]. Clinical assessments included demographic data, as follows: age, sex, weight and height, body mass index (BMI; weight [in kilograms] divided by height [in meters] squared), disease duration, and extraarticular manifestations (history of uveitis). The clinical activity was evaluated using the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) [13] and the functional score Bath Ankylosing Spondylitis Functional Index [14]. For inclusion in this study, a BASDAI ≥40/100 (corresponding to an active period of the disease) was required. Erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) levels were used as laboratory parameters of inflammation. Biological assessment also included human leukocyte antigen (HLA) B determination for the presence of HLA-B27. Patients excluded from the study were those with diabetes mellitus or other endocrine disorders (Cushing syndrome, thyroid diseases), those who were obese (BMI >30 kg/m^2), those who were underweight (BMI <18 kg/m^2), or those with liver disease. To avoid TNF-α antagonist treatment as a confounding factor, patients under or who had previously received anti–TNF-α agents were also excluded from this study. Only 2 postmenopausal women participated in the study. The treatments given (nonsteroidal anti-inflammatory drugs, second-line treatments) were also recorded. No patient had psoriasis, inflammatory bowel disease, or history of reactive arthritis.

2.1.2. Controls

The control group included 35 healthy white subjects age- and sex-matched to the patients (hospital staff, no postmenopausal woman) and without a history of inflammatory conditions or metabolic or endocrine disorders. The exclusion criteria were the same as those in the patient group.

All the subjects involved in this study gave their informed consent.

Because body composition may be influenced by physical activity and dietary intake, specific questionnaires were given to the studied subjects:

2.1.3. Physical activity

Physical activity was assessed for patients and controls using a simplified and validated questionnaire evaluating the maximum oxygen consumption (V_{O_2}max). This questionnaire established by Huet et al [15] is simple, easy to use, reliable, and correlates highly with measured V_{O_2}max. It gives the mean and usual energy expenditure expressed as estimated V_{O_2}max (in milliliters per minute per kilogram).

2.1.4. Food intake questionnaire

To appreciate eating patterns of our patients and controls, we used a short food frequency questionnaire. Food intake was evaluated during 3 consecutive days (Sunday, Monday, and Tuesday), and each food intake during these 3 days was noted in a special questionnaire. The response for each food group may be no intake or 1, 2, or more intakes daily. This questionnaire included different food groups and evaluated food consumption frequencies but not the size of the meals. The questionnaire was then examined by a nutritionist of our hospital (Mrs Nicolini Stéphanie) who calculated the calorie intake (in kilocalories per day). This short-term questionnaire gave a good evaluation of energetic intake that could be obtained by a complete diet history interview. It is simple, easy to use, validated, and available on the Web site of *l'Agence Française de la Sécurité Sanitaire des Aliments* (www.AFSSA.fr) [16].

3. Methods

3.1. Adipose tissue

A total body scan was performed using a Lunar DPX-IQ densitometer (Lunar, Madison, WI). Measurements were

given for body composition from the total body scan with fat mass (in grams) and lean mass (also in grams). The reproducibility of total body measurements was 0.7%.

3.1.1. Ghrelin, adipokines, and anabolic hormone determinations in patients and controls

After overnight fasting, venous blood samples were taken at 8:00 AM from each patient and control; and the serum was stored at −20°C. For TNF-α assessment, serum was frozen at −80°C. Leptin, adiponectin, and total ghrelin serum concentrations were measured using radioimmunoassays (Linco Research, St Charles, MO). Interassay coefficients of variation were 5.7% for leptin, 6.2% for adiponectin, and 7.9% for ghrelin. The lowest level that can be detected by each assay (sensitivity) was 0.5 ng/mL for leptin, 1 ng/mL for adiponectin, and 93 pg/mL for ghrelin. Leptin levels were adjusted for fat mass. Growth hormone, IGF-I, and insulin-like growth factor binding protein 3 (IGFBP-3, the main IGF-I binding protein) were measured by specific immunoradiometric assays (Immunotech, Marseilles, France). The between-run coefficients of variation were 6.3% for GH, 6.2% for IGF-I, and 5.7% for IGFBP-3. Insulin serum levels were also evaluated by enzyme immunoassay (AIA-Pack; Tosoh Bioscience, Tessenderlo, Belgium). Erythrocyte sedimentation rate was determined by routine laboratory procedures and fasting glycemia. Plasma CRP concentration was measured by immunonephelometry (Immage System; Beckman Coulter Instruments, Fullerton, CA). Circulating TNF-α was measured with high-sensitivity colorimetric sandwich enzyme-linked immunosorbent assay kits (R&D Systems, Lille, France) according to the manufacturer's instructions. The sensitivity was 0.12 pg/mL.

3.2. Statistical analysis

Data were expressed as mean (± SEM) and were analyzed with a computer package for statistical analysis (Alsyd; SAS, Meylan, France). Age, BMI, physical activity, results of food intake questionnaire, lean and fat masses, ESR, CRP, TNF-α, GH, IGF-I, IGFPB-3, ghrelin, and adipokines were compared between patients and controls using the nonparametric Mann-Whitney *U* test. Qualitative data were analyzed using the χ^2 test. The relationships between the different variables (BMI, fat mass, and clinical and laboratory parameters of disease activity, and ghrelin, adipokines, and anabolic hormones) were analyzed using the Spearman *r* test. A *P* value under .05 was considered significant.

4. Results

The demographics, clinical characteristics, and inflammatory markers of the studied patients are listed in Table 1. Patients and controls did not differ for age, sex ratio, BMI, levels of physical activity, and dietary intake. The CRP levels and ESR were significantly higher in patients compared with those in controls ($P < .005$), whereas serum TNF-α did not differ between the 2 groups.

Table 1
Demographics and clinical characteristics of AS patients and control subjects

	AS (n = 53)	Controls (n = 35)	P [a]
Age (y)	44.1 ± 0.6	44.6 ± 1.6	NS
Sex (male/female)	44/9	27/8	NS
BMI (kg/m^2)	26.2 ± 0.6	26.1 ± 0.8	NS
Physical activity (mL/[min kg])	35.1 ± 1.2	35.8 ± 4.2	NS
Daily calorie intake (kcal)	1725.4 ± 87.4	1573.2 ± 165.8	NS
Disease duration (y)	10.3 ± 1.3		
Axial/peripheral disease	44/9		
Extraarticular disease (uveitis) (%)	12 (22.6%)		
Ongoing treatments	NSAIDs, n = 47 Methotrexate, n = 4 Sulfasalazine, n = 7 Corticosteroids, n = 3		
BASDAI (0-100)	44.4 ± 2.8		
BASFI (0-100)	38.5 ± 3.7		
HLA-B27 (%)	46 (86.8)		
ESR (mm/h)	24.4 ± 2.8	10.5 ± 1.7	.0007
CRP (mg/L)	17.6 ± 3.1	5.0 ± 1.1	.004
TNF-α (pg/mL)	3.9 ± 1.3	1.7 ± 5.1	NS

BASFI indicates Bath Ankylosing Spondylitis Functional Index; NSAIDs, nonsteroidal anti-inflammatory drugs; NS, not significant.
[a] All tests are Mann-Whitney except for the χ^2 test for sex ratio.

We found no significant differences in fat mass and lean mass between patients and controls (all *P*s > .05, Table 2). Similarly, patients and controls did not differ significantly with respect to glycemia, insulin, GH, and IGF-I.

Circulating leptin was decreased in patients compared with controls, even after adjustment for fat mass (leptin AS vs controls, 7.6 ± 1.3 ng/mL vs 10.3 ± 1.5 ng/mL; leptin [in nanograms per milliliter]/fat mass [in kilograms], 0.28 ± 0.04 vs 0.44 ± 0.04; $P = .006$ and $P = .0003$, respectively)(Fig. 1). Because serum leptin is influenced by sex, we then examined men and women separately. We also found in male AS decreased values for circulating leptin compared with male controls (leptin, 4.45 ± 4.3 ng/mL vs 7.3 ± 3.5 ng/mL; leptin/fat mass, 0.19 ± 0.02 vs 0.37 ± 0.03; $P = .001$ and $P < .0001$, respectively), whereas in women, we found no significant differences (female AS vs female controls: leptin, 22.8 ng/mL ± 4.3 vs 20.2 ± 4.8 ng/mL; leptin/fat mass, 0.69 ± 0.11 vs 0.65 ± 0.08; all *P*s > .05) (Table 2).

Decreased values were also obtained for IGFBP-3 in AS (AS vs controls: 2.6 ± 0.1μg/mL vs 3.1 ± 0.1 μg/mL; $P < .0001$), whereas adiponectin did not differ between patients and controls (even when examining men and women separately) (Table 2).

Circulating ghrelin levels were significantly higher in patients than those in controls (1354.6 ± 70.5 pg/mL vs 1008.0 ± 82.5 pg/mL; $P = .001$) (Table 2 and Fig. 2). Results for ghrelin were also examined according to sex; and again, significant differences were found only for male patients (ghrelin male AS vs male controls: 1365.6 ± 81.5 pg/mL vs 932.8 ± 80.3 pg/mL; $P = .0006$) (Table 2).

Table 2
Fat mass, lean mass, ghrelin, adipokines, and hormonal measurements in AS and controls

	AS (n = 53) (mean ± SEM)	Controls (n = 35) (mean ± SEM)	P [a]
Fat mass (g)	21145.2 ± 1311.9	20399.3 ± 1643.2	NS
Lean mass (g)	51329.6 ± 1693.8	50943.1 ± 1670.4	NS
Glycemia (mmol/L)	4.9 ± 0.1	4.6 ± 0.1	NS
Insulin (μIU/L)	7.8 ± 0.9	7.9 ± 0.7	NS
GH (ng/mL)	2.0 ± 0.6	0.7 ± 0.2	NS
IGF-I (ng/mL)	199.0 ± 9.8	200.6 ± 10.1	NS
IGFBP-3 (μg/mL)	2.6 ± 0.1	3.1 ±0.1	<.0001
Leptin (ng/mL)	7.6 ± 1.3	10.3 ± 1.5	.006
	Men: 4.45 ± 4.3	Men: 7.3 ± 3.5	.001
	Women: 22.8 ± 4.3	Women: 20.2 ± 4.8	NS
Leptin/fat mass	0.28 ± 0.04	0.44 ± 0.04	.0003
([ng/mL]/[kg])	Men: 0.19 ± 0.02	Men: 0.37 ± 0.34	<.0001
	Women: 0.69 ± 0.11	Women: 0.65 ± 0.08	NS
Adiponectin	10.2 ± 0.7	9.5 ± 0.7	NS
(μg/mL)	Men: 9.62 ± 0.6	Men: 8.7 ± 0.7	NS
	Women: 13.3 ± 2.3	Women: 12.3 ± 1.9	NS
Leptin/	0.53 ± 0.5	0.92 ± 0.6	.02
adiponectin	Men: 0.53 ± 0.1	Men: 0.92 ± 0.1	.005
	Women: 2.02 ± 0.5	Women: 2.28 ± 0.9	NS
Ghrelin	1354.6 ± 70.5	1008.0 ± 82.5	.001
(pg/mL)	Men: 1365.5 ± 81.5	Men: 932.8 ± 80.3	.0006
	Women: 1300.9 ± 123.9	Women: 1287.3 ± 233.3	NS

[a] All tests are Mann-Whitney.

The relationships between BMI, fat mass, ghrelin, adipokines, and the parameters of disease activity were then examined. We observed a strong correlation between circulating leptin and BMI or fat mass in AS ($r = 0.76$, $P < .0001$ and $r = 0.88$, $P < .0001$, respectively) and controls ($r = 0.48$, $P = .0046$ and $r = 0.74$, $P < .0001$, respectively). On the contrary, we failed to find a correlation between adiponectin and BMI or fat mass in AS and in controls. In addition, circulating ghrelin inversely correlated with BMI and fat mass in AS patients ($r = -0.36$, $P = .01$ for both tests). Body mass index and fat mass were not correlated

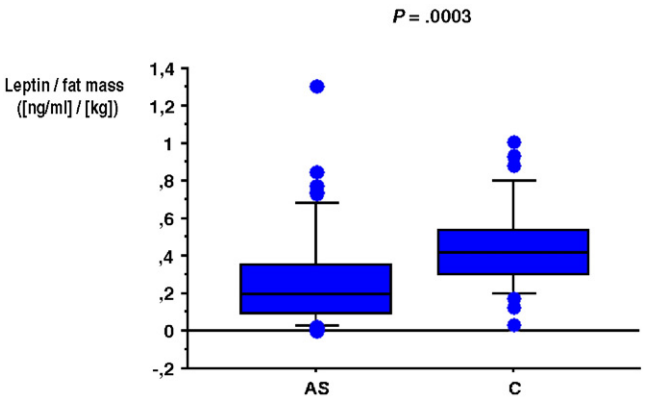

Fig. 1. Leptin serum levels adjusted for fat mass in AS and controls. C indicates controls.

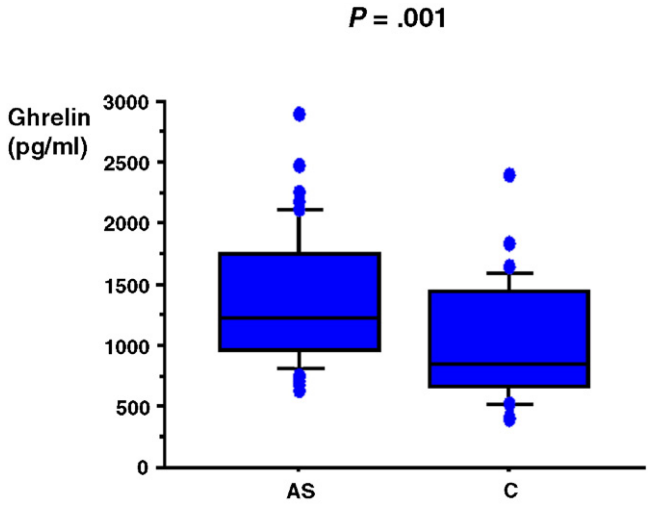

Fig. 2. Ghrelin serum levels in AS and controls.

with the biological markers of inflammation ESR, CRP, or TNF-α levels.

The relations between markers of disease activity of AS and serum levels of ghrelin and adipokines were also analyzed. We did not observe a significant correlation between serum leptin and adiponectin, and ESR, CRP, TNF-α, or BASDAI (all Ps > .05). However, serum ghrelin weakly correlated with ESR ($r = 0.29$, $P = .04$), but not with CRP or TNF-α levels (all Ps > .05).

Finally, we observed a negative correlation between IGFBP-3 and ESR and CRP ($r = -0.43$, $P = .003$ and $r = -0.35$, $P = .01$, respectively) and between IGFBP-3 and ghrelin ($r = -0.31$, $P = .025$), and a positive correlation between IGFBP-3 and leptin ($r = 0.27$, $P = .01$).

5. Discussion

Our results show that our AS patients had no changes in adipose tissue compared with controls and no changes in serum adiponectin in contrast with decreased serum leptin and increased ghrelin levels in male patients. In addition, IGFBP-3 levels were also decreased in our patients.

In inflammatory rheumatic diseases, chronic inflammation is associated with weight loss by the production of different mediators and particularly inflammatory cytokines that induce tissue damage, protein catabolism, fat mobilization, and, finally, a negative energetic balance. The risk of infection and death is highest when energy reserves are not sufficient. This situation has been described in RA as rheumatoid cachexia [1]. In RA, a recent study by our group showed that patients had decreased lean mass in contrast with normal fat mass [17]. Another study reported decreased lean mass and increased fat mass with a shift to the abdomen [18]. The loss of lean mass has been associated with disease activity, particularly inflammatory cytokines that may favor hypermetabolism, and also with corticosteroid use [1,17].

The consequences of such loss of lean mass are reduced physical activity and, thus, decreased quality of life. Another important issue is that weight loss and particularly lean mass are considered as prognostic factors for survival [1]. Two previous studies evaluated body composition in AS [19,20]; and both failed to find changes in fat mass and lean mass, suggesting an absence of or a poor relationship between disease activity, particularly inflammatory cytokines, and soft tissue composition.

Our results confirmed that AS patients had no changes in fat mass but they had reduced serum leptin. The main factor influencing serum leptin is fat mass, but these results were also observed after fat mass adjustment and were more obvious in male subjects. Indeed, in our series, serum leptin did not differ between women with AS and healthy women. These results have limitations because our series included only 9 women in the AS group and 8 in the control group. As expected, circulating leptin and adiponectin were lower in men compared with those in women. As far as we know, circulating leptin has not been previously evaluated in AS. In RA, contradictory results were obtained with normal [21,22] or elevated serum leptin levels [17,23]. Furthermore, a negative correlation between serum leptin and markers of inflammation has been found [22]. Leptin has also been investigated at the joint level in RA, and lower levels were observed in synovial fluids compared with matched serum samples. Of interest, this local leptin consumption was associated with a nonerosive course; and the authors suggested that leptin may have protective effects in RA [23]. Conversely, leptin has been implicated in the process of cartilage degradation in osteoarthritis [24]; and thus, the exact role of leptin in joint damage needs further precision. In our study, only 9 patients had peripheral disease but without joint effusion; and therefore, we were unable to analyze leptin in synovial fluids.

The primary role of leptin is to regulate appetite. However, it is still debatable whether this regulation may be explained by satiety or by signaling depletion of energy stores. Low leptin levels may induce starvation signal that can decrease physical activity. Of interest, in our series of patients, there was a trend for low physical activity and increased caloric intake, although these results were not significant.

Leptin is also implicated in regulating immunity and has several effects on immune cells from both innate and adaptive immunity: it protects T lymphocytes from apoptosis and regulates T-cell proliferation and activation; it influences cytokine production from T lymphocytes and promotes type 1 response; and it influences monocyte activation, phagocytosis, and cytokine release [7,25-27]. Our results show that male AS patients have decreased circulating leptin that was not explained by reduced fat mass, and this could constitute a regulatory mechanism to limit inflammation. Indeed, leptin deficiency has been associated with reduced inflammation in animal models of arthritis by decreasing production of proinflammatory type 1 cytokines. Alternatively, increased susceptibility to bacterial infection and suppressed lymphoproliferative responses are described in this context [25]. Therefore, reduced leptin levels in male AS may contribute to impair efficient bacterial defense.

On the other hand, it has been reported that leptin may stimulate the production of anti-inflammatory cytokines by monocytes and macrophages [28]. Macrophages from *ob*/*ob* mice show increased basal IL-6 expression, suggesting that leptin may inhibit macrophage function [29]. Leptin-deficient mice have increased mortality rates after exposure to TNF-α or lipopolysaccharide, supporting a protective role for leptin against systemic proinflammatory stimuli [29]. In the model of septic arthritis after intravenous *Staphylococcus aureus* injection, circulating leptin levels are low and leptin administration improves the arthritis without modifying the intraarticular bacterial load [30,31]. Leptin deficiency does not reduce the severity of zymosan-induced arthritis, a model in which leptin exerts anti-inflammatory effects [27]. These data indicate that leptin may protect against, or control, joint inflammation. Thus, leptin may have dual effects in modulating inflammatory response.

Adiponectin was normal in our patients. This adipokine has a primarily metabolic role by regulating insulin sensitivity; and reduced adiponectin levels are observed in obesity, dyslipidemia, and type 2 diabetes mellitus [6]. Consequently, our AS patients are probably not at high risk for metabolic syndrome. Adiponectin is also related to the inflammatory process by reducing the production of cytokines such as TNF-α and IL-6 and by inducing the release of IL-10 and IL-1 receptor antagonist [9]. In addition, leptin/adiponectin balance has been proposed as a marker for evaluating comorbidities associated with obesity, particularly obesity-associated vasculopathy and cardiovascular risk. The risk for developing atherosclerotic vascular diseases in AS has been well documented and linked to the inflammatory process. Our series of AS patients was characterized by normal adiponectin and decreased leptin levels, particularly in male patients, an adipokine profile that was suggestive of being beneficial for the risk of cardiovascular diseases. However, this should be interpreted with other classic cardiovascular risk factors such as tobacco use, dyslipidemia, and hypertension. In addition, in humans, adiponectin levels correlate negatively with fat mass in both the male and female populations. The failure to observe a relationship between fat mass and adiponectin in our patients can be explained by the inclusion of few obese patients in our study.

Ghrelin levels were elevated in our AS patients, but results were only significant for male patients. These increased ghrelin levels had no or weak influence on dietary intake because our patients had similar calorie intake compared with controls. This could be explained by a state of resistance of ghrelin as it was described for leptin in obese subjects [3,6]. Ghrelin has several physiologic functions involving GH secretion, gastric function, control of blood pressure, and adiposity. It acts as an antagonist for leptin for the regulation of satiety, stimulates appetite, and decreases

fat utilization [10]. To our knowledge, our study is the first to evaluate circulating ghrelin in AS. Ghrelin has been previously studied in RA, and decreased serum levels were found [32]. This was interpreted as a driver of rheumatoid cachexia. In our study, we observed that ghrelin negatively correlated with BMI and fat mass. In fact, serum ghrelin is high in anorexic and lean subjects and low in obese subjects [6]. Ghrelin and leptin are negatively related: leptin is able to negatively regulate ghrelin and vice versa; and thus, balance between ghrelin and leptin influences body weight [6]. In addition, it has been demonstrated that ghrelin is expressed on human monocytes and inhibits the production of inflammatory cytokines (IL-1, IL-6, and TNF-α); but it also inhibits leptin-mediated proinflammatory cytokine expression [33]. Therefore, high ghrelin and low leptin levels as observed in our patients suggest a favorable influence on the inflammatory/anti-inflammatory cytokine balance. Surprisingly, ghrelin levels correlated with ESR; but no relations were obtained with more specific markers such as CRP or TNF-α.

Taken together, our results did not show a clear relationship between circulating adipokines and (clinical or laboratory) markers of disease activity. Similar results have been reported in RA. However, it has also been demonstrated that these adipokines are present at the joint levels; and consequently, they may play a local role in AS, thereby influencing inflammation in the joints.

Finally, and as previously reported by our group [34], we found decreased IGFBP-3 levels in AS without change in IGF-I or insulin levels. Our results also show that IGFBP-3 and leptin were interrelated as previously reported [11], whereas IGFBP-3 was negatively associated with ghrelin. Decreased levels of serum IGFBP-3 could impair IGF-I activity and thus might negatively influence soft tissue and particularly lean mass. However, lean mass was normal in our series of patients; and this may be linked to the anabolic properties of ghrelin through GH and IGF-I actions.

We can conclude that AS patients had no changes in fat mass. Leptin production was reduced in contrast with normal levels of adiponectin. This fat-derived hormones profile, together with high serum ghrelin levels, may influence the inflammatory response in AS by triggering anti-inflammatory effects. However, these results were more obvious in male patients. Despite this adipokines/ghrelin balance, our patients had higher inflammation than controls, suggesting that the contribution of adipokines/ghrelin to the inflammatory process was mild. However, further studies on the fat mass distribution (abdominal and visceral fat mass) as well as the synovial production of adipokines in AS are required.

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