Prospective Assessment of Body Weight, Body Composition, and Bone Density Changes in Patients with Spondyloarthropathy Receiving Anti-Tumor Necrosis Factor-α Treatment

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ABSTRACT. ***Objective.*** To determine the changes in body weight, body composition, and bone density in patients with spondyloarthropathy (SpA) receiving anti-tumor necrosis factor-α (TNF-α) treatment.

Methods. One hundred six patients with SpA (80 men, 26 women) aged 20–71 years were included in a 2-year prospective open study. Fifty-nine patients received infliximab (3 or 5 mg/kg/infusion each 6 or 8 weeks); and 47 patients received etanercept (25 mg twice a week) because of persistent active disease despite an optimal treatment, according to ASsessments in Ankylosing Spondylitis Working Group criteria. Body weight, total body composition (lean mass, fat mass), and spine and femoral bone mineral density (BMD; dual-energy x-ray absorptiometry) were measured at baseline and at 1 and 2 years.

Results. There was a significant increase in body weight after 1 year (2.2 ± 3.9 kg, i.e., 3.4%; $p < 0.0001$) and 2 years (2.2 ± 4.7 kg, 3.5%; $p < 0.0001$), mostly due to a significant gain in fat mass at 1 year (1.4 ± 2.6 kg, 12.1%; $p < 0.0001$) and 2 years (1.5 ± 3.1 kg, 14.5%, $p < 0.0001$). Gain in lean mass was also significant at 1 year (0.8 ± 2.2 kg, 1.9%; $p < 0.0001$) and 2 years (0.9 ± 2.5 kg, 2%; $p < 0.0001$). At 2 years, lumbar spine and femur BMD increased: +5.8 ± 13% ($p < 0.0001$) and +2.26 ± 4.5% ($p = 0.001$), respectively.

Conclusion. This 2-year prospective study showed a significant increase in body weight at 1 year and 2 years, mostly due to a gain in fat mass and a significant increase in BMD, in patients with SpA receiving anti-TNF-α treatment. (First Release Mar 15 2008; J Rheumatol 2008;35:855–61)

Key Indexing Terms:
ANTI-TUMOR NECROSIS FACTOR SPONDYLOARTHROPATHY
OSTEOPOROSIS BODY COMPOSITION CACHEXIA

Cachexia, defined by a loss of skeletal muscle in the context of a chronic inflammatory disease, has been reported in rheumatoid arthritis (RA) and in spondyloarthropathy (SpA)[1-3], as in other chronic advanced diseases[4-6]. Cachexia is a consequence of a catabolic process leading to muscle atrophy and thus weakness and physical inactivity. Cachexia is linked to the disease activity of the chronic inflammatory diseases through the effects of proinflammatory cytokines such as tumor necrosis factor-α (TNF-α), interleukin 1 (IL-1), and IL-6[7,8]. TNF-α (formerly called cachectin), a pivotal cytokine in rheumatic diseases, plays an important role in the development of cachexia. TNF-α induces anorexia and increases resting energy expenditure[6,9], induces muscle loss directly by both stimulating muscle protein breakdown and reducing the sensitivity of skeletal muscle cells to anabolic stimuli[10], and downregulates the systemic and local expression of anabolic hormones and growth factors[11]. Proinflammatory cytokines (TNF-α, IL-1, IL-6) are elevated in serum of patients with SpA[12].

Anti-TNF-α therapy induces a significant and sustained reduction in clinical disease activity and systemic inflammation, and improves measures of disability in RA and SpA[13]. Anti-TNF therapy is expected to be effective to treat or prevent cachexia in patients with rheumatic disorders[11]. As expected, infusions of anti-TNF-α antibodies in animal models have shown anticachectic effects[14,15]. Recently, Marcora, *et al* reported the first randomized controlled trial of anti-TNF therapy for cachexia in RA, but did not observe changes in weight and body composition induced by this treatment in this population[11]. We have previously shown in a one-year study of 19 patients with SpA receiving anti-TNF therapy that a significant increase in weight of 2.2 kg occurred in one year in parallel with an increase in bone mineral density (BMD)[16].

In this prospective study we evaluated changes in body weight and body composition (including BMD) measured

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Accepted for publication December 16, 2007.

by dual-energy x-ray absorptiometry (DEXA) in patients with SpA receiving anti-TNF-α therapy over 2 years.

MATERIALS AND METHODS

Design. This was an open prospective 2-year followup study in one tertiary care center.

Patients. One hundred six patients (80 men, 26 women) aged 20–71 years, with SpA according to the European Spondylarthropathy Study Group (ESSG) criteria[17], 93/106 (87.8%) with ankylosing spondylitis (AS) according to the modified New York criteria[18], and 6/106 (6.6%) with psoriatic arthritis according to the criteria of the ClASsification criteria for Psoriatic ARthritis study group[19], none with reactive arthritis, were included. These patients required anti-TNF therapy because of persistent active disease despite an optimal dose of nonsteroidal antiinflammatory drug and/or treatment with methotrexate (MTX) or sulfasalazine according to either ASAS (ASsessments in Ankylosing Spondylitis Working Group) criteria (n = 72)[20], or the investigator's opinion, based on the severity of the disease (including hip joint involvement; n = 34).

Measurements. Clinical assessment included demographic data: age, disease duration, extraarticular manifestations (uveitis, inflammatory bowel disease, psoriasis), current therapies (MTX, corticosteroids). Height and weight were measured using 1 calibrated machine, at baseline and then every year. The clinical activity and severity of the disease were evaluated every 6 months for 2 years by visual analog scale (VAS) for global pain (0–100 mm), Bath AS Disease Activity Index (BASDAI), and Bath AS Functional Index (BASFI) and by biological markers of inflammation: erythrocyte sedimentation (ESR; mm/h) and C-reactive protein (CRP; mg/l).

Body composition and BMD were measured by DEXA (QDR 2000, Hologic, Waltham, MA, USA) at baseline and then once a year. BMD (g/cm^2) was determined at the lumbar spine (second to fourth vertebrae), and at the upper part of the left femur (total femur). Osteopenia was defined as a T score [number of standard deviations (SD) from the normal mean obtained from young healthy sex-matched adults] between –1 and –2.5 SD and osteoporosis as a T score ≤ –2.5 SD. BMD and body composition measurements were repeated under identical technical conditions after 1 and 2-year followup. Quality control of the device using the manufacturer's spine phantom was performed daily throughout the followup.

Intervention. All patients were treated as decided by their physician, with etanercept (25 mg twice a week) or infliximab (3 or 5 mg/kg/infusion of infliximab at Weeks 0, 2, 6, and thereafter infusions at 6 or 8-week intervals). Treatments were continued or stopped, according to usual rules in our unit (observational study design).

Statistical analysis. Analysis was performed on completed data, i.e., intent-to-treat (ITT) population (all patients were treated 2 yrs), and imputation of missing data using the last observation carried forward technique when appropriate. Changes in body weight, body composition (lean and fat mass), and lumbar spine and total hip BMD were stated as descriptive statistics, with comparisons from baseline values by t-tests or Wilcoxon signed-rank sum tests, as appropriate. Analyses were performed to explain the relative variation of weight, lean and fat mass, and BMD. For continuous explanatory variables (baseline biological and clinical variables and variations of these variables over followup) the association was tested using the Spearman correlation coefficient. For binary explanatory variables (sex, type of anti-TNF) the association was tested by t-tests or Wilcoxon signed-rank sum tests, as appropriate. Exploratory multivariate analyses were performed by multiple logistic regression, with the variable of interest analyzed in quartiles, and with as explanatory variables all variables with a p value in univariate analysis < 0.10. The analyses were performed using SAS version 9.1.

RESULTS

Baseline characteristics. The demographic, clinical, and biological characteristics of the 106 patients with SpA are listed in Table 1. Fifty-nine patients received 3 or 5 mg/kg/infusion of infliximab at Weeks 0, 2, 6, and thereafter infusions at 6 or 8-week intervals, and 47 patients received etanercept (25 mg twice a week). The body composition and BMD measurements are listed in Table 2. Few patients with SpA (6%) had a body mass index (BMI) < 19 kg/m^2. Thirty patients (28%) were osteoporotic, and 25 (23%) were osteopenic at either spine or femur. No patient reported a previous osteoporotic fracture. Five patients were taking calcium (1 g/day) and vitamin D (800 IU/day) but none were receiving anti-osteoporotic treatments.

Table 1. Baseline clinical and biological characteristics of patients with SpA (n = 106).

Characteristics	SpA (n = 106)
Age, yrs (mean ± SD)	38 (11)
Sex (F/M)	26/80
Disease duration, yrs (mean ± SD)	16.5 (8.5)
HLA-B27, n (%)	94 (89)
Axial/peripheral disease	60/46
Psoriasis, n (%)	7 (6.6)
Inflammatory bowel disease, n (%)	13 (12.2)
Previous intake of corticosteroids, patients, n (%)	36 (33.9)
Cumulative dose prednisone equivalent, mg, mean (SD)	10,632 (8277)
Current intake of steroids	
No. patients (%)	16 (15)
Dose/day (g), mean (SD)	9 (5.5)
Current intake of methotrexate	
No. patients (%)	21 (19.6)
Dose/week, mean (SD)	10 (7)
VAS pain (0–100), mean (SD)	63.6 (20.4)
BASDAI, mean SD	61.2 (19.2)
BASFI, mean SD	64.3 (22.3)
ESR, mm/h, mean (SD)	28.6 (19.9)
CRP, mg/l, mean (SD)	29 (31.7)
Weight, kg, mean (SD)	68.1 (9.5)
BMI, kg^2, mean (SD)	26 (3)
Cumulative dose of infliximab, mg, mean (SD)	2847 (846)
Cumulative dose of etanercept, mg, mean (SD)	5450 (2298)

SpA: spondyloarthropathy; VAS: visual analog scale; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BASFI: Bath AS Functional Index; ESR: erythrocyte sedimentation rate; CRP: C-reactive protein; BMI: body mass index.

Table 2. Baseline body composition and bone mineral density (BMD) measurements in patients with SpA (n = 106).

Measurement	Mean (SD)
Total body, kg	
Weight	68.1 (9.5)
Lean mass	44.1 (8.6)
Fat mass	16.3 (8.3)
Lumbar spine T score	–1.3 (1.5)
Lumbar spine BMD, g/cm^2	0.95 (0.16)
Total femur T score	–1.2 (1.0)
Total femur BMD, g/cm^2	0.87 (0.13)

Effects on disease activity and systemic inflammation. After 2 years of therapy, we observed a significant improvement of the clinical measures of disease activity assessed by the global pain score (VAS), –47.6% ($p < 0.0001$), and the scores of the BASDAI (–45.8%; $p < 0.0001$) and BASFI (–44.5%; $p < 0.0001$). After 2 years, 70.8% of patients with SpA had a BASDAI score below 40, versus 32% before anti-TNF-α therapy. A significant decrease was also observed in systemic inflammation assessed by ESR, –35% ($p < 0.0001$), and CRP, –70% ($p < 0.0001$). Similar results were observed with both anti-TNF-α treatments (data not shown).

Effects on body weight and body composition. Compared to baseline, there was a significant increase in body weight after 1 year (mean 2.2 ± 3.9 kg, 3.4% ± 5.9%; $p < 0.0001$) [median 2.0 kg, interquartile range (IQR) 0–4] and after 2 years (mean 2.2 ± 4.7 kg, 3.5% ± 7.1%; $p < 0.0001$) (median 1.75 kg, IQR –1 to 4), mostly due to a significant gain in fat mass at 1 year (1.4 ± 2.6 kg, 12.1% ± 22.4%; $p < 0.0001$) and 2 years (mean 1.5 ± 3.1 kg, 14.5% ± 26.8%; $p < 0.0001$). There was no change in weight in 40 (37.7%) patients. Gain in lean mass was also significant at 1 year (mean 0.8 ± 2.2 kg, 1.9% ± 5.2%; $p < 0.0001$) (median 1.2 kg, IQR 0–2.6) and 2 years (mean 0.9 ± 2.5 kg, 2.0% ± 5.6%; $p < 0.0001$) (median 0.5 kg, IQR –0.7 to 2.1; Figure 1). Changes between the first and second year of treatment were not statistically significant. In patients with a BMI ≤ 19 kg/m^2 at baseline (n = 11), there was also a significant gain in body weight at 12 months (mean 2.1 ± 2.7 kg; $p = 0.02$) (median 3.0 kg, IQR 0–4) and at 24 months (mean 2.7 ± 2.8 kg; $p = 0.01$) (median 3.0 kg, IQR –0.5 to 5).

Similar results were obtained for men and women. There was no difference between patients with or without corticosteroids or with or without MTX (data not shown). Two-year changes in body weight, in lean mass but not in fat mass, were positively correlated with baseline values of CRP ($r = 0.26$, $p = 0.01$; $r = 0.32$, $p = 0.0016$) and ESR ($r = 0.25$, $p = 0.01$; $r = 0.31$, $p = 0.0026$), respectively (Table 3).

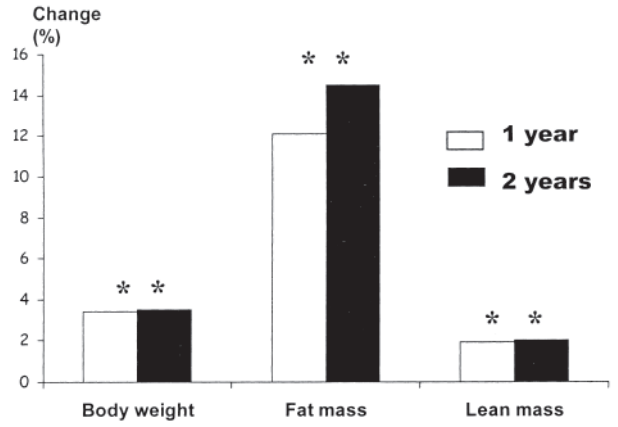

Figure 1. Relative changes (%) in body weight and body composition (lean and fat mass). *$p < 0.05$ compared to baseline.

Two-year changes in body weight and in fat mass were related to baseline body weight ($r = –0.21$, $p = 0.02$; $r = –0.30$, $p = 0.002$), respectively (Table 3). Two-year changes in body weight were correlated with the 2-year changes in fat mass ($r = 0.76$, $p \leq 0.005$) and in lean mass ($r = 0.62$, $p \leq 0.005$) (Table 3). There was no difference between patients receiving infliximab or etanercept (data not shown).

Multivariate analyses (by multiple logistic regression) showed that the weight gain was significantly explained by the weight at baseline with an odds ratio (OR) = 1.25 [95% confidence interval (CI) 1.07–1.46] ($p = 0.004$), and the 2-year changes of ESR with an OR = 1.16 (95% CI 1.03–1.30 per ESR change of 5 mm) ($p = 0.015$). Two-year changes in fat mass were significantly explained by the weight at baseline, with an OR = 1.27 (95% CI 1.09–1.48, per increase of 5 kg) ($p = 0.002$).

Effects on BMD. At 1 year there was a significant increase in spine and total hip BMD by a mean (± SD) of 3.9% ± 12.0% ($p < 0.001$) and 1.9% ± 4.3% ($p < 0.0001$), respectively. At 2 years the increases reached 5.8% ± 13.0% ($p < 0.0001$) and 2.26% ± 4.5% ($p < 0.0001$) at these 2 sites, respectively; and the 2-year values were different from both the baseline and the 1-year values ($p = 0.03$ and $p = 0.004$ for the spine, $p < 0.001$ and $p = 0.01$ for the total femur from baseline and 1 year, respectively; Figure 2). We analyzed the BMD changes among the 85 patients without lumbar syndesmophytes at baseline. There was also a significant gain in lumbar spine BMD at 12 months [+5.1% (± 6.1); $p < 0.0001$] and 24 months [+6.6 (± 8.1); $p < 0.0001$]. The gain in total hip BMD was also significant at 12 months [+2.1% (± 4.7); $p < 0.0001$] and 24 months [+2.4% (± 4.7); $p < 0.0001$].

Two-year changes in lumbar spine BMD and total hip BMD were correlated with baseline values of CRP ($r = 0.26$,

Table 3. Spearman correlation analysis of 2-year changes of body weight and body composition, baseline values (body weight, clinical activity of SpA, biological markers of inflammation) and 2-year changes.

Variables	Body Weight	Lean Mass	Fat Mass
Baseline values			
Body weight	–0.21**	0.08	–0.3***
BASDAI	–0.02	–0.04	–0.06
BASFI	0.13	0.08	0.09
ESR	0.25**	0.31***	0.17
CRP	0.26**	0.32***	0.19
Lean mass	–0.17*	–0.07	–0.08
Fat mass	–0.15	0.12	–0.40***
2-year changes			
BASDAI	–0.04	–0.06	–0.01
BASFI	0.03	–0.01	0.05
ESR	–0.07	–0.04	0.02
CRP	0.07	–0.02	0.08
Body weight	—	0.62***	0.76***
Lean mass	0.62***	—	0.33***
Fat mass	0.76***	0.33***	—

* $p < 0.10$, ** $p \leq 0.05$, *** $p \leq 0.005$. For abbreviations, see Table 1.

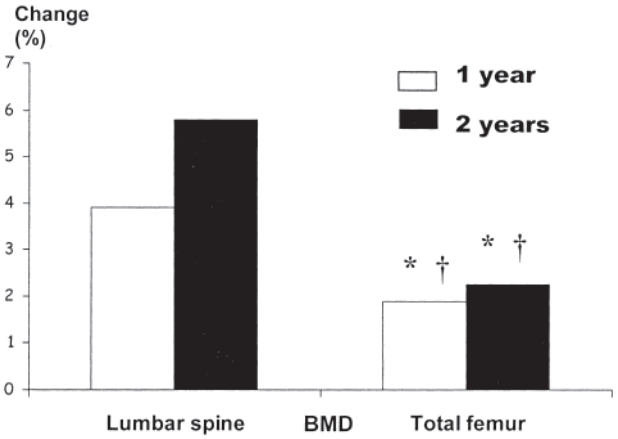

Figure 2. Relative changes (%) in bone mineral density (BMD). *p < 0.05 compared to baseline; †p < 0.05 compared to one-year results.

p = 0.01; r = 0.23, p = 0.02) and with ESR (r = 0.19, p = 0.06) only for lumbar spine changes (Table 4). Two-year changes of lumbar spine BMD and total hip BMD were also positively correlated the BMD values at baseline (Table 4). Two-year changes of lumbar spine BMD were correlated with the 2-year changes of BASDAI, BASFI, and CRP (Table 4), but were not correlated with 2-year changes in body weight and body composition. However, 2-year changes of total hip BMD were positively correlated with the 2-year increase in body weight (r = 0.4, p ≤ 0.0001), in fat mass (r = 0.31, p ≤ 0.03), and in lean mass (r = 0.25, p = 0.01) (Table 4). Two-year changes of total hip BMD were also correlated to 2-year changes of CRP (Table 4). There was no difference in these changes between infliximab and etanercept–treated patients (data not shown).

Multivariate analyses (by multiple logistic regressions) showed that the 2-year changes in lumbar spine and total femur BMD are significantly explained by the baseline value of lumbar spine BMD, with an OR = 1.45 (95% CI 1.1–1.9, per increase of 0.1 g/cm^2; p = 0.005), and total femur BMD, OR = 1.42 (95% CI 1.02–1.97, per increase of 0.1 g/cm^2; p = 0.038), respectively.

Table 4. Spearman correlation analysis of 2-year changes of lumbar spine and total hip bone mineral density (BMD), baseline values (body weight, clinical activity of SpA, biological markers of inflammation) and to 2-year changes.

Variables	Lumbar Spine BMD	Total Hip BMD
Baseline values		
Body weight	0.2	0.1
BASDAI	–0.12	–0.18*
BASFI	0.14	0.10
ESR	0.19*	0.15
CRP	0.26**	0.23**
Lumbar spine T score	–0.44***	–0.17*
Total femur T score	–0.12	–0.33***
2-year changes		
Body weight	0.19	0.4***
BASDAI	0.19**	–0.12
BASFI	0.23**	–0.02
ESR	0.15	0.09
CRP	0.2**	0.21**
Lean mass	0.20	0.25***
Fat mass	0.16	0.31***

* p < 0.10, ** p ≤ 0.05, *** p ≤ 0.005. For abbreviations, see Table 1.

DISCUSSION

This open prospective study conducted in patients with SpA receiving anti-TNF-α (etanercept or infliximab) shows a significant gain in body weight (mean 2.2 kg) with significant changes of body composition after 1 and 2 years of treatment. The gain of weight was mainly due to a gain of fat mass, although the increase of lean mass was also significant. Moreover, we confirmed the benefit of treatment by anti-TNF-α on BMD (+5.8%) in patients with SpA over 2 years.

Marcora, *et al* recently provided evidence of cachexia in 19 patients with longstanding and active SpA: although they had similar values of body weight and BMI, patients with SpA had a lower lean mass (–6 kg) than controls[1]. In patients with RA, cachexia is linked to a loss of body mass cells and is not associated to a loss of body weight; most patients have a normal BMI and even an excess of fat mass, a condition called "cachectic obesity"[21]. In our study, the mean value of BMI was 26 kg/m^2 and only 6% of patients had a BMI below 19 kg/m^2. In the absence of a control group, we could not determine the proportion of SpA patients with cachexia in our study; moreover, we did not measure other cardinal features of cachexia such as an elevated basal metabolic rate or an accelerated muscle protein breakdown[21]. Our data show that the absolute increase in body weight was of similar magnitude in patients with low BMI (i.e., < 19 kg/m^2) or high BMI. Consequently, we could not say that the patients with a severe disease and a more reduced weight gained more weight than the patients with a normal weight at baseline. Our data indicate that the weight gain during the anti-TNF therapy is of similar magnitude through the range of baseline body weights.

The weight gain and the body composition changes we observed in patients with SpA receiving anti-TNF treatment may be explained by a specific effect of anti-TNF-α therapy or by the generic effects of inflammation control by anti-TNF-α therapy, or both. The positive effects of anti-TNF-α treatment on weight and body composition can be mediated by improvements in well-being, appetite, and physical activity through control of disease activity. We did not measure physical function, but an improvement in physical activity cannot explain the early gain in weight and the body composition changes observed in the first weeks or months of anti-TNF therapy. Moreover, we have previously shown that the increase of weight was mainly observed during the first 6 months of anti-TNF treatment[16], and we observed in this study that there was no more weight gain during the second year of followup.

These significant changes can be related to a specific effect of anti-TNF-α because of the known effects of TNF-α in the development of cachexia in chronic diseases: reducing gastric emptying and peristalsis[22], inducing lipolysis, inhibiting lipid synthesis[23], and increasing proteolysis[24-26]. Moreover, animal studies showed that infusions of anti-TNF-α antibodies have anticachectic effects[14,15]. Experimental studies conducted in animals and humans showed that TNF-α induces a transient increase of leptin during acute inflammation and decreases leptin release during chronic inflammation[27,28]. One injection of infliximab (5 mg/kg) in patients with Crohn's disease induced a significant increase of leptin levels after 1 and 4 weeks[29]. However, Marcora, *et al* showed that MTX, a disease modifying antirheumatic drug (DMARD) used in RA, is as effective as etanercept to limit cachexia in RA[11], suggesting the role of control of inflammatory disease activity by the therapy. This hypothesis could also explain the early gain in weight and the body composition changes observed in the first weeks or months of anti-TNF therapy. In 20 patients with active Crohn's disease, one injection of infliximab (5 mg/kg) was associated with an increase in body weight as early as 4 weeks after the injection[29]. These observations are in favor of a direct relationship with inflammation control. In our previous study, we observed early changes in biological measures, including a significant increase in serum insulin-like growth factor-I concentration at 3 months, which returned to baseline value at 6 months. This phenomenon may be related to a transient reduction in the growth-hormone resistance associated with systemic inflammation[16]. Thus, we hypothesize that such a mechanism may explain our results in patients with SpA.

Our 2-year prospective open study confirms previous data on bone density improvement in patients with SpA treated by anti-TNF[30,31]. The 1-year changes in BMD reported in our study were of similar magnitude to the 6-month changes in BMD observed in 29 patients receiving infliximab (+3.3% at lumbar spine and +2.2% at total hip)[31,32]. Bone loss is a frequent complication during the course of SpA, and longitudinal studies in early SpA have shown that lumbar spine and total hip BMD decreases predominantly in patients with active disease[33]. In our study, an increase in BMD was observed in parallel with a decrease in systemic inflammation resulting from TNF-α inhibition. We studied the correlation between changes in ESR and CRP and BMD changes at 2 years, and we found a correlation between the 2-year changes in lumbar spine BMD and total hip BMD and the 2-year changes in CRP (Table 4). We reported in a preliminary study[34] that a large and sustained decrease of bone resorption (assessed by a serum marker) was observed during anti-TNF therapy. Together, these data suggest an indirect effect of anti-TNF therapy on bone, through control of the inflammation-related bone resorption.

We observed an increase in lumbar spine BMD after 1 year and 2 years of followup. Several hypotheses may explain these results. Correction of a mineralization defect can result in a large increase in BMD; however, serum calcium and phosphorus were normal in all patients (data not shown) and we have no data suggesting a subclinical underlying osteomalacia at baseline. Moreover, we did not give vitamin D to these patients. A study in experimental murine colitis suggested that TNF-α downregulates the osteoblast Phex gene expression, a phosphate-regulating gene involved in the mineralization process, but the relevance of these results *in vivo* are still unknown[35]. We found a correlation between the increase of body weight and femur BMD, but not with spine BMD. This has been shown in healthy adults and in postmenopausal women, suggesting the role of mechanical factors; femoral neck density is related to lean mass, possibly through the effects of weight-bearing exercise on both of these measures[36,37]. In contrast, this effect is less on lumbar spine BMD as this part of the skeleton, mainly of trabecular histology, is more dependent on hormonal[38-40] or inflammatory[41,42] effects. However, an improvement in physical activity may have a positive effect on lumbar spine BMD, through the direct effects on spine of posterior muscles[43] and psoas[44]. We did not measure physical activity in our patients, but this improvement has been reported in patients with SpA receiving anti-TNF therapy[13]. Finally, the lumbar spine BMD measured by DEXA in AS can be falsely increased by the presence of lumbar syndesmophytes[45]. We cannot eliminate the occurrence of syndesmophytes in some patients to explain the increase in lumbar spine BMD as we did not perform radiographs at the end of the followup in asymptomatic patients, and we recognize that there may be a discrepancy between clinical improvement and structural changes[46]. TNF decreases osteoblastic activity through both Wnt, a secreted protein involved in bone formation, and bone morphogenetic protein pathways; thus anti-TNF may improve osteoblastic activity, leading to an increase in systemic bone formation (with an increase in BMD), but may not have a positive structural effect in patients with SpA[47]. However, the changes in lumbar spine BMD were similar in patients with and without lumbar syndesmophytes at baseline, and the changes at the femur were of similar magnitude compared to those at the spine. Other techniques such as quantitative computerized tomography (QCT) have been proposed to avoid measurement of syndesmophytes while measuring lumbar spine BMD[48]. Our data suggest that DEXA is a relevant tool for the followup of patients with AS receiving anti-TNF therapy.

Our study has strengths and limitations. Patients were followed in a single center with standardized procedures for all the outcomes. Body composition and BMD by DEXA were performed in the same laboratory by the same investigator. The duration of the study was longer than in previous studies. We recognize that the absence of a control group precludes any definitive conclusion; however, we were

unable to find a relevant control group for patients having severe active disease and requiring anti-TNF therapy. In particular, we cannot conclude that the observed effect is specific to the anti-TNF therapy and would not be present with any active DMARD. Finally, the large increase in weight and fat mass we observed calls for assessment of serum lipids in further studies.

Our study showed a significant increase in body weight, mostly due to a gain in fat mass, in patients with SpA after 1 and 2 years of treatment with anti-TNF-α. We confirm the benefit of anti-TNF-α therapy on bone density in a large cohort of patients with SpA over 2 years.

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