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Progressive vertebral deformities despite unchanged bone mineral density in patients with sarcoidosis: a 4-year follow-up study

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Abstract

Summary To evaluate the incidence of new and/or progressive vertebral deformities and changes in bone mineral density, we re-examined 66 patients with sarcoidosis after a follow-up period of four years. In 17 subjects (26%) new and/or progressive vertebral deformities were found, though BMD did not change significantly.

Introduction Previous studies from our group have shown that morphometric vertebral deformities suggestive of fractures can be found in 20% of patients with sarcoidosis, despite a normal bone mineral density (BMD). The aim of this study was to determine the incidence of new and/or progressive vertebral deformities and the evolution of BMD during the course of this disease.

Methods BMD of the hip (DXA) and vertebral fracture assessment (VFA) with lateral single energy densitometry was performed at baseline and after 45 months in 66 patients with sarcoidosis. Potential predictors of new/progressive vertebral deformities were assessed using logistic regression analysis.

Results The BMD of the total group was unchanged after follow-up. The prevalence of vertebral deformities increased from 20 to 32% (p<0.05); in 17 subjects (26%) new or progressive vertebral deformities were diagnosed. A lower T-score of the femoral neck [(OR=2.5 (CI: 1.0-5.9), p<0.05)] and mother with a hip fracture [(OR=14.1 (CI:1.4-142.6), p<0.05)] were independent predictors of new/progressive deformities.

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Conclusions In subjects with sarcoidosis the number of vertebral deformities increases in the course of this disease, despite unchanged BMD. The combination of low normal BMD and family history of fragility fractures confers an increased risk of the incidence of these deformities.

Keywords Bone mineral density · Sarcoidosis · Vertebral deformities

Introduction

Sarcoidosis is a T-cell driven chronic inflammatory disease. Although chronic inflammation has been associated with decreased bone mineral density as a result of the effects of cytokines on bone metabolism [1–4], we and others could not demonstrate changes in BMD in subjects with this condition, even if treated with glucocorticoids (GCs). In a cross-sectional study of 124 subjects with sarcoidosis, BMD values similar to an age- and sex-matched reference population were found [5]. Comparable observations were made in three small studies in untreated patients [6–8]. These studies also found a normal BMD relative to age and sex-matched controls, except for a small group of postmenopausal women in which BMD was moderately decreased at the spine in longstanding sarcoidosis only [7].

Although in our cross-sectional study normal BMD values were observed, increased levels of the bone resorption marker serum carboxy-terminal cross-linked telopeptide of type I collagen (ICTP) and the bone formation marker serum procollagen type I amino-terminal propeptide (PINP) suggestive of increased bone turnover were found [5]. ICTP levels correlated with markers of disease activity such as soluble IL-2 receptor (sIL2R) and angiotensin converting enzyme (ACE). In addition, vertebral deformities suggestive of fracture were demonstrated in 20% of the subjects studied in this series. This may imply that the fracture risk in sarcoidosis is increased due to an increased bone turnover with consequent changes in microarchitecture and decrease of bone strength which is not reflected by changes in BMD [9, 10].

If so, this may result in progressive vertebral deformities during the course of the disease. For this reason we re-examined individuals with sarcoidosis four years after the initial measurements to determine the incidence of new and/or progressive vertebral deformities and their relation with changes in BMD.

Subjects and methods

Subjects

Sixty-six of the 124 subjects with sarcoidosis that were studied in 2002 [5] agreed to participate in the follow-up study performed in 2006. None of the 56 subjects who declined or were unable to participate had impaired mobility or a history of vertebral fractures. The mean age of this group was 45 years and did not differ with respect to gender or glucocorticoid (GC) use from the group of subjects that were re-examined in 2006.

Demographic, clinical and treatment data of the subjects studied in 2002 and 2006 are summarized in Table 1. The group consisted of 22 pre-menopausal women, 11 post-menopausal women, and 33 men; median age of the total group (all Caucasian) was 43 years (20–66 y). The clinical records of all patients were reviewed. In 2002 patients were evaluated according to a standard protocol that included questionnaires, measurement of height and weight, lung function, measurement of BMD, a single energy densitometry of the spine, and laboratory evaluation [5]. In 2006 the same protocol was repeated. Informed consent was obtained from all participants and the study was approved by the medical ethics committee of our institution.

Pulmonary evaluation

Lung function measurements, including forced expiratory volume in one second (FEV1) and forced vital capacity (FVC), were measured with a pneumotachograph. The diffusion capacity for carbon monoxide (DLCO) was measured using the single-breath method (both Masterlab, Jaeger, Würzburg, Germany). Values were expressed as a percentage of those predicted [11].

Chest radiographs were graded according to the radiographic staging of DeRemee (0 to III), adding stage IV, the end stage of lung fibrosis [12, 13]. All interpretations were made by a radiologist who was blinded to the patient's history.

Laboratory assays

Serum 1,25-dihydroxyvitamin D concentration was determined by radioimmuno-assay using a commercially available kit [(IDS Ltd, Boldon, England, interassay coefficient of variation (IE-CV) 18%, intra-assay CV (IA-CV) 15%)]. High-sensitivity C-reactive protein (hs-CRP) was measured by particle-enhanced immunonephelometry on the BN Prospec (Dade Behring). The detection limit is 0.175 mg/L

Table 1 Baseline and follow-up demographic, clinical, and treatment variables (n=66)

Variable	Baseline (n=66)	Follow-up (n=66)	$P*$
Demographic variables			
Female sex	33 (50%)		
Postmenopausal	11 (17%)	14 (21%)	ns
Age, years	43 (20–66)		
Body mass index, kg/m^2	26.9±5.7	27.2±5.3	ns
Smoking	7 (11%)		
Daily dietary calcium intake, mg	740 (110–2360)	758 (150–1340)	ns
Clinical variables			
Disease duration, years	3 (1–22)	7 (5–26)	
Chest X-ray stage (0-I-II-III-IV)	24/11/12/16/3	27/5/12/15/7	ns
FEV1,% of predicted	87±28	91±26	ns
DLCO,% of predicted	87±16	92±18	ns
Physical activity	8.6±3.7	8.1±3.7	ns
Laboratory values (in serum)			
Calcium, mmol/l (2.1–2.6)	2.4±0.1	2.4±0.08	ns
1,25(OH)2D3, nmol/l (0.040–0.200)	0.14±0.03		
ACE, U/l (9–25)	22.5±9.8	15.3±7.9	0.001
sIL-2R, kU/l (241–846)	654 (188–4315)		
Hs-CRP, mg/l (<10)	3.2 (0.2–191)	2.0 (1–16)	<0.05
Z-score ICTP	0.7±1.4		
Z-score PINP	−0.1±0.9		
Treatment variables			
GC use never	31 (47)	26 (39)	ns
GC use previous	14 (21)	25 (38)	<0.01
GC use current	21 (32)	15 (23)	ns
Lifetime GC dose, mg	9240 (200–48750)	11187 (200–56700)	<0.001
Daily dose, mg	12.4±6.2	10.5±3.3	<0.05
Started on bisphosphonates after baseline measurement		6 (9)	
Clinical risk factors for osteoporosis			
Fracture	2 (2/24=8%)	5 (5/28=18%)	ns
Low body weight (< 60 kg)	8 (12)	7 (11)	ns
Severe immobilization	0	0	ns
Low physical activity index ≤ 5	18 (27)	18 (27)	ns
Mother with hip fracture	6 (9)	7 (11)	ns

Data are given as mean ± SD, median (range) or number (%); *=p value between baseline and follow-up measurement. Reference parameters in brackets

Abbreviations: GC, glucocorticoid; FEV1, forced expiratory volume in one second; DLCO, diffusion capacity for carbon monoxide; 1,25(OH)2D3, 1,25 dihydroxyvitamin D; ACE, angiotensin converting enzyme; sIL-2R, soluble interleukin-2 receptor; Hs-CRP, high-sensitivity C-reactive protein; ICTP, carboxy-terminal cross-linked telopeptide of type I collagen; PINP, procollagen type I amino-terminal propeptide

and the measuring range is 0.175–1100 mg/L. Soluble IL-2 receptor (sIL-2R) was determined on the IMMULITE automated analyzer, by means of a two-site chemiluminescent enzyme immunometric assay with a measuring range of 50–7500 kU/L (Diagnostic Product Corporation, Los Angeles, CA, cat no LKIP1). Serum angiotensin converting enzyme (ACE) was measured using a colorimetric method. The precision of the ACE assay was < 5.6% and the reference interval for ACE was 9–25 U/L.

As a marker for bone formation, serum procollagen type I amino-terminal propeptide (PINP) was measured. As a marker for bone resorption, serum carboxy-terminal cross-linked telopeptide of type I collagen (ICTP) was assessed. Both PINP (IE-CV 3.2%, IA-CV 2.5%, lowest detectable concentration 0.4 μg/l) and ICTP (IE-CV 3.5%, IA-CV 2.3%, lowest detectable concentration <0.1 μg/l) were measured using commercial RIA kits (Orion Diagnostica Oy, Espoo, Finland). To adjust for age and gender Z-scores for these bone markers were obtained using a Dutch reference group (300 women, 150 men), checked for normal BMD of the lumbar spine and femur and normal 25-hydroxyvitamin-D levels [14, 15].

Bone mineral density and vertebral morphometry

Bone mineral density (BMD) was measured by dual X-ray absorptiometry (DXA, Hologic QDR 4500). In 2002 only the BMD of the hip was measured. In 2006 the BMD of both the hip and of the lumbar spine were determined. As reference group for the hip the NHANES III database (sex- and age-matched) was used. A standard protocol as described previously was used for measurement of BMD. To adjust for age and gender, Z-scores were used. To examine changes in Z-scores between baseline and follow-up measurements a Δ Z-score was calculated reflecting the difference between the Z-score at follow-up and the Z-score at baseline.

Furthermore, after bone density measurement a lateral single energy densitometry of the thoracic and lumbar spine for vertebral fracture assessment (VFA) was performed (also called Morphometric X-ray absorptiometry (MXA)) [16]. The scans obtained were analyzed twice by one trained operator (intra-observer correlation: 0.85), using the semi-quantitative method of Genant [17]. In addition we measured every vertebra quantitatively. The observer was blinded to the T-score values and to the values of the first set of measurements. After visual examination six points were placed on each vertebral body from T4 to L4. From these points three vertebral heights were measured anterior (Ha), mid (Hm) and posterior (Hp). On the basis of the average score of these morphometric measurements, ratios were calculated and a prevalent vertebral deformity was defined as a reduction of height of 20% or more (Ha/Hp; Hm/Hp and Hp/Hp below). Severity of deformities was assessed using the scoring system of Genant [17]. A score of '0' was assigned to normal, non-fractured vertebra; '1' for a mild deformity (20–25% reduction in anterior, middle or posterior vertebral height); '2' for a moderate deformity (25–40% reduction) and '3' for a severe deformity (>40% reduction). A new vertebral deformity was scored if a normal vertebra (grade 0) became deformed (grade ≥ 1) and a progressive deformity if the grade increased [17].

Questionnaires

Calcium intake of all patients was scored in 2002 as well as 2006 on the basis of a detailed dietary list. Known clinical risk factors for osteoporosis (weight below 60 kg, mother with hip fracture, history of fractures after age 50, menopausal status and severe immobilization) as well as daily activities and exercise were assessed by a validated questionnaire [18], in which sports, daily and work activities are scored with a minimum of zero and a maximum of eighteen. GC therapy was evaluated by means of a patient questionnaire and verified using all the records of the patient's pharmacist. It was scored as never, previous or current use and if subjects were currently using GCs, the daily dose was noted.

Statistics

Student t-tests, chi-square tests, and one-way ANOVAs were used, depending on the variables and subgroups tested. Depending on the analysis, change scores or actual scores were used. Patients with new and/or progressive vertebral deformity were clustered for the multivariate and the receiver-operating characteristics (ROC) analysis. Multivariate logistic regression analyses was performed to assess the strength of association between the incidence of new and/or progressive vertebral deformities and gender, age, weight, clinical risk factors, GC use, lifetime GC dose, daily GC dose, disease activity, bone markers, calcium intake, physical activity and BMD measurements. The variables that were entered in the multivariable analysis were those variables that appeared related ($p < 0.10$) to this outcome measure in univariate analyses. Odds ratio (OR)

Table 2 BMD variables at baseline and follow-up for the total group (n=66, median follow-up duration 45 months (range 35–49 months)

Variable	Baseline measurement	Follow-up measurement	P*
BMD, mean ± SD gm/cm2			
Femoral neck	0.84±0.12	0.83±0.12	ns
Trochanter	0.74±0.13	0.74±0.12	ns
Total hip	0.97±0.13	0.98±0.14	ns
Lumbar spine		1.04±0.14	
Z-score, mean ± SD			
Femoral neck	0.17±1.0	0.23±1.1	ns
Trochanter	0.27±1.1	0.32±1.1	ns
Total hip	0.18±1.0	0.32±1.0	0.001
Lumbar spine		0.03±1.4	
T-score, mean ± SD			
Femoral neck	−0.42±1.0	−0.46±1.0	ns
Trochanter	−0.02±1.1	−0.03±1.0	ns
Total hip	−0.14±1.0	−0.10±1.0	ns
Lumbar spine		−0.50±1.3	

Abbreviations: BMD, bone mineral density
P*=p value between baseline and follow-up measurement

and its 95% confidence intervals (CI) were calculated by using SPSS version 12.0. ROC analysis was used to assess the ability of various levels of the T-score femoral neck to predict the incidence of a new and/or progressive vertebral deformity. The ROC curve indicates the probability of a true-positive result as a function of the probability of a false-positive result for all possible threshold values [19]. A p value < 0.05 was considered statistically significant.

Results

Bone mineral density and bone turnover parameters

The results of BMD measurements are shown in Table 2. The BMD of the total group remained unchanged after a median follow-up of 45 months (range 35–49 months). When stratifying patients according to GC use, no decrease in each of the subgroups was found. Patients that never used GCs showed a Δ Z-score of the femoral neck (FN) of 0.03 ± 0.36 and a Δ Z-score of the trochanter of -0.08 ± 0.37. In patients with previous use of GCs these Δ Z-scores were 0.10 ± 0.36 and 0.22 ± 0.43, respectively. Even the group currently on GCs revealed no decrease of Z-score (Δ Z-score FN: 0.06 ± 0.30 and Δ Z-score trochanter: 0.00 ± 0.18) and also the subgroup of postmenopausal women (n=11) did not show significant bone loss (Δ Z-score FN: 0.06 ± 0.45 and Δ Z-score trochanter: -0.05 ± 0.52). In the total group, bone turnover parameters at baseline showed an increased Z-score of ICTP compared to norm scores (0.7, 95% confidence interval (CI):0.4–1.1; p<0.001). on the other hand, the marker of bone formation (Z-score PINP) did not differ from the reference population.

Clinical fractures and vertebral deformities

Three new non-vertebral fractures occurred during the follow-up period. These included a hip fracture (twice in the same patient), an ankle fracture and a fracture of the thumb. All these fractures were related to trauma and occurred in subjects older than 50 years.

Table 3 Number and grade of deformities

	Baseline	Follow-up
No. of subjects with deformity	13 (20%)	21 (32%)*
No. of deformities		
Mild	17	28
Moderate	2	8
Severe	0	0
Total	19	36

*P<0.05 between number of subjects with deformity at baseline and follow-up

Morphometric data are summarized in Table 3. In 2002 vertebral deformities (ratio of <0.80) were found in 19 vertebrae of 13 subjects. Seventeen of these were wedge and two biconcave deformities. No crush deformities were seen. The majority of these deformities were found in the low thoracic region. At follow-up a new vertebral deformity was scored if a normal vertebra (grade 0) became deformed (grade ≥ 1) and a progressive deformity if the grade increased [17]. With this method, 36 vertebral deformities were found in 21 subjects. In one subject a vertebral deformity (ratio 0.78 of T11) found in 2002 was not found at follow-up (ratio 0.81). So, in total nine new subjects revealed one or more vertebral deformities, which means an increase of vertebral deformities from 20 to 32% of the subjects studied (p<0.05). From the 21 subjects with a vertebral deformity in 2006, 17 subjects (26% of total group) were diagnosed with one or more new or progressive vertebral deformities and in four subjects the deformity was unchanged compared to baseline. Data on number and severity of the deformities can be found in Table 3. Six patients were started on a bisphosphonates after baseline measurement and from these six patients, two had a new or progressive vertebral deformity at follow-up.

Comparing the groups with and without new or progressive vertebral deformities at follow-up, no differences in Δ Z-scores of BMD of the trochanter or femoral neck (FN) were found (Δ Z-score trochanter -0.02 ± 0.41 and 0.08 ± 0.38 respectively and Δ Z-score FN 0.01 ± 0.32 and 0.08 ± 0.35). In addition no differences in baseline Z-scores of ICTP and PINP were seen between these groups. Multivariable logistic regression analysis, including factors that correlated in the univariate analysis, revealed that a T-score of the femoral neck at baseline (OR per 1 SD T-score reduction=2.5 (CI: 1.0–5.9), p=0.04), and a mother with a hip fracture (OR=14.1 (CI:1.4–142,6), p=0.02) were determinants of a new and/or progressive morphometric vertebral deformity at follow-up measurement. Factors such as age, gender, calcium in take, GC use, daily GC dose, lifetime GC dose, disease activity, bone markers, radiographic stage and disease duration at baseline did not predict new and/or progressive vertebral deformities.

The threshold level of the T-score FN that maximized the combined specificity and sensitivity on the ROC curve (Fig. 1) was < −0.45 for predicting a new and/or progressive deformity (sensitivity 88%, specificity 51%).

Discussion

In this cohort of subjects with sarcoidosis, a high prevalence of morphometric vertebral deformities suggestive of fracture was found, as well as a substantial increase in vertebral deformities during a follow-up period of four

years. In 2002 20% of subjects were diagnosed with vertebral deformities according to the criteria of Genant [17], which increased to 32% of all subjects in 2006. In parallel, the total number of deformities in these subjects almost doubled. However, BMD of the trochanter and femoral neck did not change over time and BMD of the lumbar spine at follow-up measurement did not differ from the reference population. These data are suggestive of an increased risk of progressive vertebral deformities in individuals with sarcoidosis despite preservation of BMD.

Although data on prevalent or incident fractures in younger healthy populations are lacking, data from other studies suggest that the incidence and prevalence of vertebral deformities in this population are indeed high. Prevalence rates of 30% asymptomatic vertebral fractures are demonstrated in elderly post-menopausal women on chronic GC therapy using the same techniques [20]. In a previous study in 60 subjects (mean age 49±13 years) with differentiated thyroid carcinoma we found vertebral deformities in 7% of patients [21]. Data from the European Vertebral Osteoporosis Study (EVOS), a very large cross-sectional population based study on European subjects aged 50 to 79 years, showed a prevalence of vertebral deformities of 12% (range 6–21%) in males and females [22]. In the Rotterdam study, in which 3469 men and women aged 55 years and older were studied, the prevalence of vertebral deformity suggestive of fracture was 6.9% in men and 7.5% in women [23]. The epidemiology of vertebral fractures in women aged 50–54 years turned out to vary in different countries from 4.7% – 11.5% [24]. All these studies indicate that the fracture risk in subjects with sarcoidosis is substantial, regardless the differences in populations studied and differences in methodology.
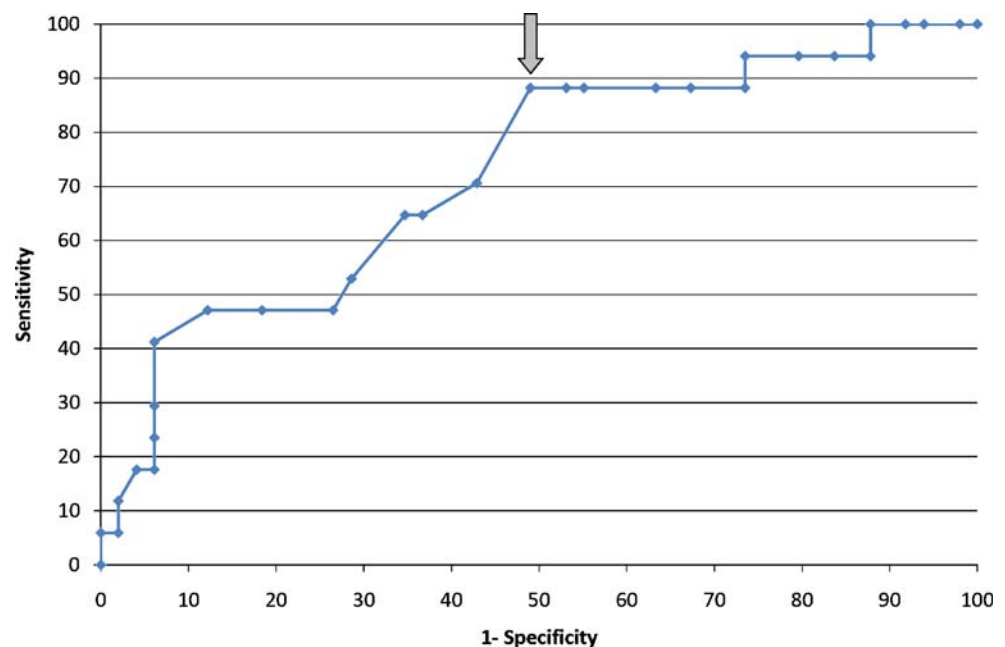
A new vertebral deformity was found in 15 subjects (23%). To identify incident deformities several approaches can be followed. Measurement of changes in vertebral heights of the same vertebral body from a baseline to a later radiograph in which a decrease in height of 15 or 20% or 4 mm is suggestive of fracture [25, 26], changes in indices of vertebral area [27] or changes in the number or presence of prevalent deformities [17, 28]. Black and coworkers evaluated these different approaches and concluded that none of these were consistently better than any other method [29]. As we aimed to assess the change of numbers of subjects with one or more vertebral deformities over time we used the last method [17], in which changes in number of prevalent deformities are scored. A comparable approach was followed in the European Prospective Osteoporosis Study (EPOS) [30], which revealed an incidence of new deformities of 3.4% after a similar follow-up period. As the mean age of subjects included in this study was substantially higher than that of our cohort, these data cannot be used as a reference, although it is likely that in younger age groups even lower incident deformities would be observed. The high prevalence of vertebral deformities at baseline, the significant increase of more than 50% of subjects after follow-up with one or more deformity and the increase of severity of prevalent deformities all imply that sarcoidosis is a relevant risk factor for vertebral deformity.

What is the underlying mechanism of this predisposition to vertebral deformities in view of the lack of effects on BMD in sarcoidosis? The load bearing capacity of bone, also referred to as 'whole bone strength', depends on the amount of bone, the spatial distribution of the bone mass, and the intrinsic properties of the materials that comprise the bone. Thus, properties at the cellular, matrix, micro- and

Fig. 1 ROC curve using Femoral neck T-score to identify patients with new and/or progressive vertebral deformity. Area under the curve (AUC): 0.72. *Arrow*: The threshold level of T-score FN that maximized combined specificity and sensitivity was < −0.45 (sensitivity 88%, specificity 51%)

macro-architectural levels may all impact the mechanical properties of bone [31, 32]. Apparently, in sarcoidosis mechanisms are involved that influence bone strength without having a significant impact on bone mass. As we found in the total group an increased marker of bone resorption (Z-score ICTP) at baseline, one of the possible mechanisms could be increased bone remodelling with a negative effect on bone micro-architecture that is not reflected by a change in BMD. It is well known that chronic inflammatory diseases influence bone physiology by the production of cytokines stimulating bone turnover [1, 2, 33]. Increased bone remodelling is associated with an increased bone fragility and thus fracture risk [34, 35] and in postmenopausal women the level of bone turnover turned out to be an as strong and independent predictor of fractures as BMD [36, 37]. These data may support the hypothesis that the chronic inflammatory state in sarcoidosis results in increased bone remodelling with a negative effect on bone strength and thus an increased fracture risk.

No changes in BMD in the group currently treated with GCs were found. This is unexpected as GCs are known to effect BMD via several mechanisms with consequent decrease of BMD. It may well be that this is due to intermittent GC use, as most of our patients were on intermittent glucocorticoids. Other studies have demonstrated that intermittent GC use has no major effects on BMD [38]. A recent large retrospective cohort study on clinical fracture risk among patients from the UK General Practice Research Database showed that intermittent use of high dose of oral GCs was associated with only a small increase in the risk of osteoporotic fractures [39].

Despite the on average normal BMD, we found T-score of the femoral neck and a family history of hip fractures to be predictors of a new and/or progressive vertebral deformity. This suggests that the combination of a lower BMD in combination with the increased bone turnover in sarcoidosis predisposes to progressive vertebral deformity. If so, this would mean that in these high risk individuals preventive treatment should be considered to reduce fracture risk. Controlled trials are needed, however, to substantiate this suggestion.

One of the limitations of our study is the lack of an age and sex matched control population. Unfortunately data on vertebral deformities in younger populations are at present not available. The aim of this study was, however, not to compare sarcoidosis patients with healthy subjects, but to follow a cohort of these patients and to compare follow-up with baseline measurements. Another limitation is the use of morphometric X-ray absorptiometry (MXA) instead of spine radiographs. MXA is less reliable for the detection of deformities at the upper thoracic spine, where deformities are less frequent as compared to the lumbar and mid-thoracic spine. A recent study comparing MXA with lateral spine X-ray found that vertebral morphometry using MXA allowed diagnosis of vertebral fracture in the lumbar and mid thoracic spine, where vertebral fractures are most common [40]. The advantage of MXA is the low dose of radiation and the convenience of the technique for patients. The present quality of the images, with ongoing refinement of this technology, is considered sufficient to be used for the diagnosis of vertebral deformity consistent with fracture [41]. Furthermore there is a lack of a "gold standard" for VFA. We followed the method of Genant [17], which is based on a reduction of the ratios of anterior, middle or posterior heights and all measurements were performed twice to improve accuracy. This is the simplest and most practical method [42] and an association with future fracture risk is documented [43, 44]. The above mentioned EVOS study, however, applied the methodology described by McCloskey and Eastell and co-workers in which measurements are corrected for normal variations in vertebral shape [25]. Relative to the method of Genant, the method of Eastell [25] or McCloskey [28] may have resulted in lower prevalences of vertebral deformities. This does not, however, explain the differences in prevalence of vertebral deformities reported elsewhere and in this paper. The restrictions of the methodology are also the limited ability to provide a differential diagnosis for the detected deformities, a lower sensitivity for milder fractures and the inability to evaluate the uppermost thoracic levels. Other disorders that may cause changes in vertebral shape involve congenital abnormalities and conditions as severe osteoarthritis [45] and Scheuermann's disease. We have, however, no indications that these relatively rare conditions may have interfered with our observations.

In conclusion, we have shown that in subjects with sarcoidosis the number of vertebral deformities, diagnosed with morphometric assessment, increases during the course of this disease despite preservation of BMD. Although this is an uncontrolled study, it appears that subjects with sarcoidosis have an increased fracture risk, even if BMD is normal. High risk individuals can be identified by a low-normal BMD and by a family history of hip fractures. Probably these individuals will benefit from therapies that increase bone strength. A T-score FN below −0.45 may be used to identify these individuals with a high sensitivity and an acceptable specificity. Studies evaluating the effects of such therapies in individuals with sarcoidosis are however clearly needed.

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