Chapter 4

High frequency of vertebral fractures in early Spondylarthropathies

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Abstract

Summary: We demonstrated that vertebral fractures (VF) are commonly found in early SpA. Patients with VF had lower lumbar BMD than patients without VF. VF remained frequently 'unrecognized' and untreated. VF have been associated with more back pain, reduced Qol and increased risk of future fractures which stresses the importance of recognition also in early stage SpA.

Introduction: VF are a common complication of longstanding Ankylosing spondylitis (AS). However, data of VF in early AS patients and in other Spondylarthropathies (SpA) are scarce. Therefore we examined the prevalence of VF in early SpA patients and investigated the associations between VF and demographic and disease-related variables.

Methods: SpA patients were included consecutively and radiographs of the spine were made. VF were assessed according to the method of Genant et al.: fractures were defined as reduction of ≥20% of the vertebrae. Descriptive statistics, t-tests and logistic regression analyses were used to study the relationship between VF and demographic and disease-related variables, radiographic damage and BMD.

Results: A total of 113 early SpA patients were included with a disease duration of 7 months, a mean age of 37 years. Seventeen patients (15%) had at least one VF. Fourteen patients had one VF, three patients had two VF. Most VF were located at Th6–Th8. In patients with VF, bone mineral density (BMD) of lumbar spine was lower than BMD of patients without VF (t-test: p=0.043). Axial Psoriatic arthritis (PsA) was significantly associated with a higher risk for VF (OR 4.62, 95% CI 1.15–18.58, p=0.031). No significant associations were found with disease activity variables nor with radiographic severity.

Conclusion: In a group of 113 early, young SpA patients, 15% already had at least one VF. Most VF were asymptomatic, undetected by routine diagnostic procedures and located at the mid-thoracic spine. The VF were associated with low BMD of the lumbar spine and with axial PsA.

Introduction

Spondylarthropathies (SpA) include a group of chronic inflammatory diseases that consists of Ankylosing spondylitis (AS), Psoriatic arthritis (PsA), Reactive arthritis, arthritis or sacroiliitis associated with inflammatory bowel diseases, undifferentiated Spondylarthropathies and Juvenile Spondylarthropathies. SpA are characterized by involvement of the sacroiliac joints and the axial skeleton, but also by enthesitis and peripheral arthritis. Extra-articular manifestations of the eyes (acute anterior uveitis), skin (psoriasis) and gut (Crohn's disease and Ulcerative colitis) often occur. AS is the major subtype of the SpA group of diseases since it has clear classification criteria for many decades now, and many clinical and epidemiological studies relating to this disease have been published unlike other types of SpA.

Loss of bone mass (osteopenia and osteoporosis) is a well recognized feature of longstanding and severe AS [1–4]. Due to the continual bone resorption as well as the reduced capacity of shock absorption, the ankylosed and rigid spine is at risk of developing fractures and becoming increasingly deformed [1]. Vertebral compression fractures due to osteoporosis are therefore a common and serious complication of longstanding AS [1, 5]. These fractures frequently occur spontaneously or after minor trauma and are associated with mortality and morbidity through neurological complications, decreased physical function, increased kyphosis and more back pain [6, 7].

In mild and earlier forms of AS, a high incidence and prevalence of low bone mineral density (BMD) was also described [3, 4, 8] but only a few studies are available on BMD in other types of SpA. Previously, we showed that low BMD in early stage SpA is highly common in this population (47%) [9]. However, data on vertebral fractures in early AS, but also in other Spondylarthropathies, are scarce. Vertebral fractures are important to be studied, for they are often overlooked in daily clinical practice, and because of the association with above mentioned complications and increased risk of future vertebral and non-vertebral fractures [10–12]. Therefore, we assessed the prevalence of vertebral fractures in SpA patients at an early stage of disease and investigated the association between vertebral fractures, and demographic, disease-related and BMD-related variables.

Patients and methods

Study population

The study group consisted of patients aged ≥18 years with inflammatory back pain [13] and a recent diagnosis of Spondylarthropathy (according to the European Spondylarthropathy Study Group [ESSG] criteria) [14]. The diagnosis Spondylarthropathy consisted of AS, Undifferentiated SpA, patients with inflammatory back pain and, Psoriatic arthritis (PsA), inflammatory bowel diseases, or Reactive arthritis and Juvenile SpA [14]. All patients were consecutively enrolled in a prospective early Spondylarthropathy study at Reade, a large outpatient rheumatology clinic in the Netherlands. The local Medical Ethics Committee approved the study protocol and all participants gave written informed consent.

Data collection

A verified medical history, physical examination, and laboratory assessment were obtained from all SpA patients at inclusion. Radiographs (of the lateral cervical, thoracic and lumbar spine) and DXA scans were made according to protocol. Few patients of which radiographs were missing or not made at the time of the DXA scan (±3 months) were excluded. The following patient characteristics were collected: demographic data (e.g., gender, date of birth), disease-related variables like symptom duration (time of first complaints until inclusion), disease duration (moment of diagnosis until inclusion) and history of peripheral arthritis, inflammatory bowel diseases, psoriasis and uveitis. In addition, the disease activity score, BASDAI (Bath Ankylosing Spondylitis Disease Activity Index) [15], the functional capacity scores, BASFI (Bath Ankylosing Spondylitis Functional Index) [16] and BASMI (Bath Ankylosing Spondylitis Metrology Index) [17], were collected. Laboratory assessment included erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) and the presence of the HLA-B27 antigen. BMD-related variables were also obtained, like 25-hydroxy vitamin D levels, data on previous peripheral fractures, menopausal status, and medication i.e., use of anti-osteoporotic or disease-modifying anti-rheumatic drugs (DMARDs), corticosteroids and tumor necrosis factor alpha blocking agents (anti-TNF).

Radiological damage of the cervical and lumbar spine (lateral) was assessed by two readers (IvdH and CvD) according to the modified Stoke Ankylosing Spondylitis Spine Score (mSASSS) [18]. The inter-observer variability was calculated by means of the intraclass correlation coefficient (ICC=0.93).

BMD of the lumbar spine (L2-L4) and left proximal femur was measured with DXA equipment (Lunar DPX-IQ, Madison, WI, USA) and the results were presented as BMD (g/cm^2), T-scores and Z-scores. The T-score corresponds to the number of standard deviations (SD) from any result of the peak bone mass, and the Z-score is the T-score with a correction for age and weight. The definitions of the World Health Organization (WHO) were used to define osteoporosis (T-score ≤-2.5 in the spine and/or hip), osteopenia (-2.5< T-score <-1.0 in the spine and/or the hip, without osteoporosis) and normal bone density (T-score ≥-1.0 in both sites) [19].

Outcome measure

The primary outcome measure in this study was vertebral fractures. Vertebral fractures were assessed at lateral radiographs of the thoracic and lumbar spine (T5–L4) using the standardized semi-quantitative method described by Genant et al. [20]. In Genant et al.'s semi-quantitative assessment, vertebrae receive a severity grade based on the visually apparent degree of vertebral height loss. Reduction in height is divided in grades on a scale of 0 to 3; grade 0 (normal) represents a reduction in anterior, middle and/or posterior vertebral heights of less than 20%, grade 1 (mild) represents a reduction of 20-25%, grade 2 (moderate) represents a reduction of 25-40% and grade 3 (severe) more than 40% reduction. Vertebral fractures were defined as reduction of ≥20% of the vertebral body height [20]. The scoring procedure was performed by two experienced readers (BD and WL). The very few discrepancies that were observed were additionally scored by a third person, and consensus was reached.

Statistical analysis

Data were expressed as means (with standard deviations) or medians (with interquartile ranges) as appropriate. Demographic properties of all subjects and characteristics of disease activity were summarized by descriptive statistics. Differences in characteristics between SpA patients with vertebral fractures and without vertebral fractures were evaluated by using independent t-tests for normally distributed variables, Mann–Whitney U-tests for skewed variables and Pearson χ^2 tests for dichotomous variables. Univariate and multivariate logistic regression analyses were performed to investigate associations between disease-related factors and the presence of vertebral fractures (p-values <0.05 were

considered statistically significant). The software used was SPSS for windows, version 15.0.

Results

Characteristics of the early SpA cohort

A total of 113 patients were included and their characteristics are summarized in Table 1.

Table 1. Characteristics of 113 patients with an early SpA

	N=113
Demographic variables	
Men[a]	75 (66)
Age[b], (years)	37.3 (9.0)
Types of Spondylarthropathies	
Ankylosing spondylitis[a]	80 (71)
Undifferentiated Spondylarthropathy[a]	12 (11)
SpA and Inflammatory bowel disease[a]	5 (4)
Reactive arthritis[a]	5 (4)
Psoriatic arthritis[a]	10 (9)
Juvenile Spondylarthropathy[a]	1 (1)
Disease related variables	
Disease duration[c], (months)	7.2 (2.1-14.4)
Symptom duration[c], (years)	5.7 (2.0-11.6)
HLA-B27, (positivity)[a]	85 (75)
CRP[c]	4.0 (2.0-12.0)
BASDAI[b], (0-10)	4.2 (2.3)
BASFI[c], (0-10)	2.3 (0.9-4.6)
BASMI[c], (0-10)	1.0 (0.0-2.0)
Uveitis[a]	26 (23)
Psoriasis[a]	10 (9)
Inflammatory bowel disease[a]	5 (4)
Peripheral arthritis[a]	37 (33)
mSASSS[c], (0-72)	2.0 (1.0-4.7)

CRP= C-Reactive Protein, BASDAI= Bath Ankylosing Spondylitis Disease Activity Index, BASFI= Bath Ankylosing Spondylitis Functional Index, BASMI= Bath Ankylosing Spondylitis Metrology Index, mSASSS= modified Stoke Ankylosing Spondylitis Spinal Score. [a]Number (%), [b]Mean (SD), [c]Median (IQR).

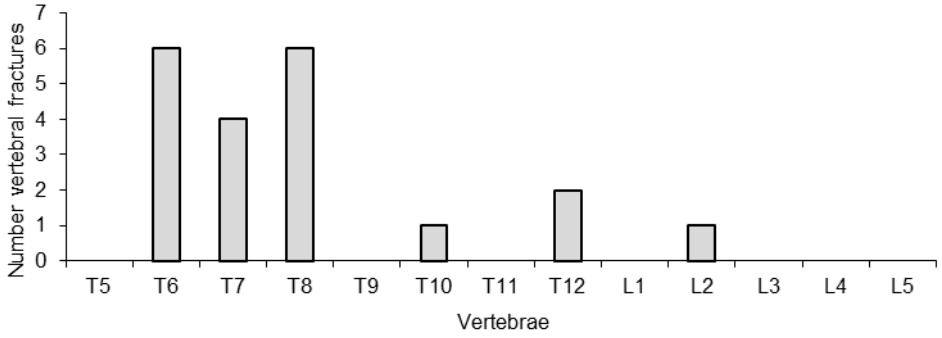
The patient group consisted for 71% of AS patients, 66% was male and the median disease duration was 7.2 months after diagnosis. Almost all patients used non-steroidal anti-inflammatory drugs (NSAIDs) (95%), and only 5% was treated with a DMARD and 2%

with a biological. None of the patients used corticosteroids or bisphosphonates. All women included in this study were premenopausal.

Outcome measure vertebral fractures

In 17 patients (15%), at least one vertebral fracture (grade 1 or higher) was found; 14 of these patients had one vertebral fracture and three had two vertebral fractures but none had more than two. All fractures were wedge deformities. In total, ten grade 1 fractures were detected and ten grade 2 fractures, but no grade 3 fractures were found. Most vertebral fractures were located at the mid-thoracic spine (n=16, Th6-Th8) and low-thoracic spine (n=3, Th10-Th12), only one at the lumbar spine (L2) (Figure 1).

Figure 1. Location of vertebral fractures



Of the 17 patients with a vertebral fracture, four patients were clinically diagnosed as such ('some reduction in height'), but in the 13 other patients the vertebral fractures were undetected by the radiologist.

The different types of Spondylarthropathies in which vertebral fractures were present are described in Table 2.

Table 2. Vertebral fractures in different types of spondylarthropathies

Types of SpA	Patients with VF
Ankylosing spondylitis (N=80)	9 (11%)
Axial Psoriatic arthritis (N=10)	4 (40%)
AS and Inflammatory bowel disease (N=5)	1 (20%)
Undifferentiated Spondylarthropathy (N=13)	3 (23%)

Differences between patients with and without vertebral fractures

Comparison of characteristics between patients with and without vertebral fractures revealed that patients with vertebral fractures were more often male and were somewhat older (Table 3). Further, the cumulative disease activity, as indicated by ESR, CRP and BASMI score was slightly higher in the group of patients with vertebral fractures. However all these parameters were not significantly different between the two groups.

BMD of the hip did not differ significantly between those with and without vertebral fractures. However, BMD of the lumbar spine was significant lower for the vertebral fractures group than the non-vertebral fractures group (t-test; p=0.043). The T-score and Z-score of the lumbar spine showed the same trend (t-test; p=0.057 vs. p=0.112).

Osteoporosis was present in eight out of 113 patients (7.1%) in hip and/or spine. Seven patients had osteoporosis of the spine, two patients of the hip and one of both hip and spine. Three of these eight osteoporotic patients had a vertebral fracture. This means that 14 out of 17 patients with a vertebral fracture did not have osteoporosis based on a low T-score.

Osteopenia was detected in 43 out of 113 patients (38.1%) in this early stage of disease. When combining patients with osteoporosis and/or osteopenia (low BMD), 51 patients (45.1%) had low BMD whereas 62 patients (54.9%) had normal BMD. The number of vertebral fractures (n=9) in the 51 patients with low BMD (17.6%) was only moderately higher compared with the number of fractures (n=8) in the 62 patients with normal BMD (12.9%). Therefore, out of 17 patients with a vertebral fracture, only nine (52.9%) had low BMD (osteopenia and/or osteoporosis) and the other half (eight patients (47.1%) showed just a normal BMD.

Previous non-vertebral fractures (fractures due to small accidents in childhood or adolescence) were slightly higher in patients with vertebral fractures compared to those without (52.9% vs. 38.5%), however this did not differ significantly. Also, other fracture associated variables like body mass index and vitamin D levels did not differ between patients with and without fractures. Radiological damage (mSASSS) in the total SpA group was very low with a median score of 2.0 (1.0-4.7), confirming that this was an early SpA group. There was no difference in radiographic damage between the group with and without fractures.

Use of NSAIDs, DMARDs, corticosteroids, biologicals and bisphosphonates did not differ between the two groups. In both groups, almost all patients used NSAIDs. Of the 17 patients with vertebral fractures, two patients used a DMARD and no patient had ever used

corticosteroids, biologicals or bisphosphonates. In the group without vertebral fractures, four patients used a DMARD and two patients used a biological. All patients with vertebral fractures or with a T-score ≤-2.5 had never used bisphosphonates.

Table 3. Characteristics of SpA patients with and without vertebral fractures

	VF (N=17)	No VF (N=96)	P-value
Demographic variables			
Men[a]	13 (76)	62 (65)	0.339
Age[b], (years)	40.8 (10.0)	36.7 (8.7)	0.083
Disease-related variables			
Disease duration[c], (months)	4.6 (0.3-10.2)	7.6 (2.7-15.7)	0.101
Symptom duration[c], (years)	3.9 (1.2-11.6)	5.7 (2.1-11.7)	0.368
Ankylosing spondylitis[a]	9 (53)	71 (74)	0.079
ESR[c]	12.0 (3.0-28.5)	8.0 (5.0-19.0)	0.798
CRP[c]	8.0 (1.5-17.0)	4.0 (2.0-12.0)	0.341
BASDAI[b], (0-10)	4.1 (2.4)	4.2 (2.3)	0.813
BASFI[c], (0-10)	1.7 (0.9-3.7)	2.4 (0.9-4.8)	0.930
BASMI[c], (0-10)	2.0 (1.0-2.5)	1.0 (0.0-2.0)	0.293
Uveitis[a]	1 (6)	25 (26)	0.069
Psoriasis[a]	4 (24)	6 (6)	**0.021**
Inflammatory bowel disease[a]	1 (6)	4 (4)	0.751
Peripheral arthritis[a]	9 (53)	28 (29)	0.143
Other BMD-related variables			
BMI[b], (kg/m^2)	24.5 (4.8)	24.8 (3.5)	0.717
Vitamine D[b], (nmol/l)	54.8 (19.1)	59.9 (21.7)	0.376
Previous non-vertebral fractures[a]	9 (53)	37 (39)	0.265
mSASSS[c], (0-72)	2.8 (0.5-4.6)	2.0 (1.0-5.0)	0.829
BMD variables			
sBMD hip[b]	0.945 (0.081)	0.961 (0.121)	0.591
sBMD L2-L4[b]	1.054 (0.192)	1.140 (0.154)	**0.043**
T-score hip[b]	-0.5 (0.8)	-0.3 (1.0)	0.431
T-score L2-L4[b]	-1.0 (1.7)	-0.2 (1.4)	0.057
Z-score hip[b]	-0.4 (0.8)	-0.3 (1.0)	0.678
Z-score L2-L4[b]	-0.9 (1.7)	-0.3 (1.4)	0.112

ESR= Erythrocyte Sedimentation Rate, CRP= C-Reactive Protein, BASDAI= Bath Ankylosing Spondylitis Disease Activity Index, BASFI= Bath Ankylosing Spondylitis Functional Index, BASMI= Bath Ankylosing Spondylitis Metrology Index, mSASSS= modified Stoke Ankylosing Spondylitis Spinal Score, BMI= Body Mass Index. [a]Number (%), [b]Mean (SD), [c]Median (IQR).

Associations between vertebral fractures and disease-related variables

Univariate analysis shows that SpA patients with vertebral fractures had lower BMD and T-scores of the lumbar spine and had more often psoriasis. Psoriasis proved to be significantly related with vertebral fractures (odds ratio [OR] 4.62, 95% confidence interval [CI] 1.15-18.58, p=0.031). All patients with psoriasis and a vertebral fracture turned out to be patients with the diagnosis (axial) Psoriatic arthritis (PsA). These were mainly cases with axial PsA from the non-AS group (other SpA than AS) who had vertebral fractures. BMD of the lumbar spine and the T-score were significantly associated with vertebral fractures (although the T-score borderline), (OR 0.993, 95% CI 0.993-1.000, p=0.047 vs. OR 0.701, 95% CI 0.483-1.016, p=0.061).

Subgroup analyses for gender showed that CRP was significantly higher in women with vertebral fractures compared to women without fractures (OR 1.10, 95% CI 1.01-1.20, p=0.040). Further subgroup analyses showed that mainly male patients with non-AS diseases had vertebral fractures (OR for AS was 0.15, 95% CI 0.04-0.53, p=0.004), and in this subgroup of males it were especially the patients with axial PsA (OR 6.44, 95% CI 1.36-30.47, p=0.019).

Subgroup analysis for AS vs. other types of SpA showed that in the non-AS group, high BASMI (OR 3.75, 95% CI 1.37-10.74, p=0.011), low BMD of the lumbar spine (OR 0.99, 95% CI 0.98-1.00, p=0.012), low T-score of the lumbar spine (OR 0.26, 95% CI 0.09-0.74, p=0.011) and low Z-score of the lumbar spine (OR 0.20, 95% CI 0.05-0.82, p=0.025) were all significantly related with vertebral fractures.

Discussion

The present study demonstrates a high prevalence of vertebral fractures (15%) in relatively young patients with different types of SpA at an early stage of disease. Vertebral fractures were associated with a low BMD of the lumbar spine and with the presence of axial PsA. Most vertebral fractures were found in the mid-thoracic spine and the majority was not detected by specific symptoms or clinical routine examination.

The high number of vertebral fractures (15%) in this early SpA group, with a median disease duration of 7 months, is interesting because it equals the number of fractures detected in patients with longstanding or severe AS (0-18%) [21], which is often associated with low BMD. The low radiographic damage score in our group, with a median mSASSS

score of only 2.0 (IQR 1.0-4.7) out of a maximum score of 72, supports the observation that our group consists of early SpA patients.

Limited data are available on studies of vertebral fractures in early AS. Mitra et al. studied a small number of patients with mild AS (n=66) and found a high prevalence (16.7%) of vertebral fractures in AS compared to 2.6% in healthy controls, which is in accordance with our results [3]. The fact that most fractures in our early SpA group were low-grade (grade 1 or grade 2) suggest that low grade vertebral fractures are probably already present at an early stage of disease, while high grade fractures are more typical for longstanding disease [22].

Many studies show that one of the highest risk factors to develop vertebral fractures is low BMD, especially osteoporosis [22, 23]. This is in contrast with our findings in early SpA, which shows that the majority of patients with vertebral fractures (82%) do not fulfill the criteria for osteoporosis. BMD, measured by DXA of the spine, is often a matter of dispute in AS because it often shows relatively high T-scores due to severe calcifications of the ligaments and syndesmophyte formation compared with measurements of the femur. However, this usually occurs in populations with longer disease durations and does not apply to our early SpA population, with a disease duration of 7 months and minimal radiographic changes. Again our results are consistent with previous findings of Mitra et al. [3], who also demonstrated a lack of association between vertebral fractures and BMD of the hip.

Apart from BMD, other known risk factors for vertebral fractures, like vitamin D deficiency, low body mass index and a history of previous non-vertebral fractures did not reveal any association with vertebral fractures in our early SpA group, which could be masked by the relatively low number of patients and the short disease duration. Further the gender association, which is limited by the low percentage of women in this study (34%), showed that significantly more male patients of the non-AS group were prone to have a vertebral fracture, especially in the axial PsA group. Of course it could be that male patients suffer from more severe SpA, as shown in the PSOAS cohort in AS patients [24] and we also observed more radiographic damage in our male SpA patients (data not shown). However, overall there was no significant difference in radiographic damage between patients with and without a vertebral fracture. The prevalence of 15% vertebral fractures in these young and predominantly male early SpA patients, is clearly higher than the percentage of 2.6% in healthy controls described by Mitra et al. [3] or 6-7% found in Dutch

males of the general population of 55-59 years old [25]. However, the interpretation of the prevalence of vertebral fractures is limited by the absence of an age and gender matched control group, and the fact that it is a known phenomenon that vertebral fractures do occur in young men, related to sport injuries and traffic accidents. Therefore, all patients were asked about relevant trauma or major accidents, but none of the patients with vertebral fractures reported them. Besides that, we also showed a relation between vertebral fractures and low BMD and, interestingly, these fractures were predominantly located at the same parts of the spine as in typical osteoporotic fractures: the mid and low thoracic spine, which also suggests a role for underlying osteoporosis in these patients. The high prevalence of especially 'mild' VF in the thoracic spine in AS was recently also confirmed by Montala et al. [26]. The interpretation of the prevalence of vertebral fractures is further limited by the fact that the method of Genant does not differentiate between the aetiology of the reduction of vertebra height: AS-related deformities, degenerative changes or osteoporotic compression fractures. Nevertheless, other causes but osteoporosis are less likely because loss of height in patients with degenerative changes usually occurs in less than 20% and vertebral changes due to severe AS are not expected due to the minimal radiographic damage in our early SpA patient group.

As far as we know, no studies concerning vertebral fractures have been performed in different types of SpA; however, very few were performed in AS patients with also associated conditions (psoriasis, inflammatory bowel diseases) [8, 27]. The study of Donnelly et al. [23] detected vertebral fractures in nine out of 87 patients (10.3%) with longstanding AS and/or other associated conditions. Interestingly, we found in our study a relatively high prevalence (24%) of vertebral fractures in axial PsA patients. Although we are aware of the small numbers, this may be an interesting finding. Peri-articular osteoporosis is well recognized in PsA [28], studies on systemic bone loss however are scarce and conflicting: some report systemic osteoporosis [29, 30], but others do not [31–33]. Even less information is available concerning vertebral fractures in (axial) PsA patients. However, since (axial) PsA has clinical features in common with RA (poly-articular disease) as well as with AS (axial component), this is an intriguing finding, although further larger studies are needed to confirm this observation.

Apart from the association with axial PsA, we could not detect any other clinical parameter (like extra-articular manifestations or radiographic progression) or disease activity

parameters (like ESR and CRP or BASDAI and BASFI) that could explain the presence of the vertebral fractures.

Moreover, most vertebral fractures (76.5%) were not detected by physicians and radiologists in routine radiology measurements [34, 35]. Next to chronic back pain, that might lead to misinterpreting the symptoms of a vertebral fracture, these patients were relatively young (mean age 37 years) and predominantly male and are therefore not considered to be a typical high-risk group for vertebral fractures, which reduces the chance of detection. This problem was also recognized by Geusens et al. [36] as they described several reasons for which diagnosing vertebral fractures is difficult in AS. The fact that most fractures in our study were located in the thoracic spine might be another explanation for the fact that most fractures were missed in clinical routine procedures, partly due to the over projection of the heart and lungs. Therefore, we conclude that X-rays of the thoracic spine, in addition to the cervical and lumbar spine, should be incorporated in follow up procedures of SpA patients in order to detect these vertebral fractures. Knowledge of existing fractures is necessary for the optimal assessment of risk for future fractures [34, 37, 38] as the presence of a vertebral fracture increases the relative risk of this independently of the BMD [39–41]. It is noteworthy that none of our patients with a vertebral fracture received treatment against osteoporosis, but on the other hand no optimal treatment strategy has been developed yet for treatment of vertebral fractures in the SpA population.

With the present study, we have demonstrated that, especially in mid and low thoracic spine, vertebral fractures are commonly found in early SpA patients. Patients with vertebral fractures had significantly lower lumbar BMD than SpA patients without vertebral fractures, but the majority did not fulfill the criteria of osteoporosis. The vertebral fractures in our study population remained frequently ‘unrecognized’ and untreated. Vertebral fractures have been associated with more back pain, reduced quality of life, and increased risk of future vertebral and non-vertebral fractures [10, 11, 39], which stresses the importance of recognition of these fractures in daily practice also in early stage of disease. Optimal treatment strategies of these patients may pose a challenging topic for future research.

Reference list

[1] Bessant R, Keat A (2002) How should clinicians manage osteoporosis in ankylosing spondylitis? J Rheumatol 29:1511–1519.

[2] El Maghraoui A, Borderie D, Cherruau B, Edouard R, Dougados M, Roux C (1999) Osteoporosis, body composition, and bone turnover in ankylosing spondylitis. J Rheumatol 26:2205–2209.

[3] Mitra D, Elvins DM, Speden DJ, Collins AJ (2000) The prevalence of vertebral fractures in mild ankylosing spondylitis and their relationship to bone mineral density. Rheumatology (Oxford) 39:85–89.

[4] Will R, Palmer R, Bhalla AK, Ring F, Calin (1989) Osteoporosis in early ankylosing spondylitis: a primary pathological event? Lancet 2:1483–1485.

[5] Karberg K, Zochling J, Sieper J, Felsenberg D, Braun J (2005) Bone loss is detected more frequently in patients with ankylosing spondylitis with syndesmophytes. J Rheumatol 32:1290–1298.

[6] Altenbernd J, Bitu S, Lemburg S, Peters S, Seybold D, Meindl R et al (2009) Vertebral fractures in patients with ankylosing spondylitis: a retrospective analysis of 66 patients. Rofo 181:45–53.

[7] Vosse D, Feldtkeller E, Erlendsson J, Geusens P, van der Linden S (2004) Clinical vertebral fractures in patients with ankylosing spondylitis. J Rheumatol 31:1981–85.

[8] Cooper C, Carbone L, Michet CJ, Atkinson EJ, O'Fallon WM, Melton LJ III (1994) Fracture risk in patients with ankylosing spondylitis: a population based study. J Rheumatol 21:1877–1882.

[9] Van der Weijden MA, van Denderen JC, Lems WF, Heymans MW, Dijkmans BA, van der Horst-Bruinsma IE (2011) Low bone mineral density is related to male gender and decreased functional capacity in early spondylarthropathies. Clin Rheumatol 30:497– 503.

[10] Briggs AM, Greig AM, Wark JD (2007) The vertebral fracture cascade in osteoporosis: a review of aetiopathogenesis. Osteoporos Int 18:575–584.

[11] Schuit SC, van der Klift M, Weel AE, de Laet CE, Burger H, Seeman E et al (2004) Fracture incidence and association with bone mineral density in elderly men and women: the Rotterdam Study. Bone 34:195–202.

[12] Lems WF (2007) Clinical relevance of vertebral fractures. Ann Rheum Dis 66:2–4.

[13] Calin A, Porta J, Fries JF, Schurman DJ (1977) Clinical history as a screening test for ankylosing spondylitis. JAMA 237:2613–2614.

[14] Dougados M, van der Linden S, Juhlin R, Huitfeldt B, Amor B, Calin A et al (1991) The European Spondylarthropathy Study Group preliminary criteria for the classification of spondylarthropathy. Arthritis Rheum 34:1218–1227.

[15] Garrett S, Jenkinson T, Kennedy LG, Whitelock H, Gaisford P, Calin A (1994) A new approach to defining disease status in ankylosing spondylitis: the Bath Ankylosing Spondylitis Disease Activity Index. J Rheumatol 21:2286–2291.

[16] Calin A, Garrett S, Whitelock H, Kennedy LG, O'Hea J, Mallorie P et al (1994) A new approach to defining functional ability in ankylosing spondylitis: the development of the Bath Ankylosing Spondylitis Functional Index. J Rheumatol 21:2281–2285.

[17] Jenkinson TR, Mallorie PA, Whitelock HC, Kennedy LG, Garrett SL, Calin A (1994) Defining spinal mobility in ankylosing spondylitis (AS). The Bath AS Metrology Index. J Rheumatol 21:1694–1698.

[18] Creemers MC, Franssen MJ, van 't Hof MA, Gribnau FW, van de Putte LB, van Riel PL (2005) Assessment of outcome in ankylosing spondylitis: an extended radiographic scoring system. Ann Rheum Dis 64:127–129.

[19] WHO Study Group (1994) Assessment of fracture risk and its application to screening for postmenopausal osteoporosis. Report of a WHO Study Group. World Health Organ Tech Rep Ser 843:1–129.

[20] Genant HK, Wu CY, van KC, Nevitt MC (1993) Vertebral fracture assessment using a semiquantitative technique. J Bone Miner Res 8:1137–11348.

[21] El Maghraoui A (2004) Osteoporosis and ankylosing spondylitis. Joint Bone Spine 71:291–295.

[22] Ghozlani I, Ghazi M, Nouijai A, Mounach A, Rezqi A, Achemlal L et al (2009) Prevalence and risk factors of osteoporosis and vertebral fractures in patients with ankylosing spondylitis. Bone 44:772–776.

[23] Donnelly S, Doyle DV, Denton A, Rolfe I, McCloskey EV, Spector TD (1994) Bone mineral density and vertebral compression fracture rates in ankylosing spondylitis. Ann Rheum Dis 53:117– 121.

[24] Lee W, Reveille JD, Davis JC Jr, Learch TJ, Ward MM, Weisman MH (2007) Are there gender differences in severity of ankylosing spondylitis? Results from the PSOAS cohort. Ann Rheum Dis 66:633–638.

[25] Burger H, Van Daele PL, Grashuis K, Hofman A, Grobbee DE, Schutte HE et al (1997) Vertebral deformities and functional impairment in men and women. J Bone Miner Res 12:152–157.

[26] Montala N, Juanola X, Collantes E, Munoz-Gomariz E, Gonzalez C, Gratacos J et al (2011) Prevalence of vertebral fractures by semiautomated morphometry in patients with ankylosing spondylitis. J Rheumatol 38:893–897.

[27] Vosse D, Landewe R, van der Heijde D, van der Linden S, van Staa TP, Geusens P (2009) Ankylosing spondylitis and the risk of fracture: results from a large primary care-based nested casecontrol study. Ann Rheum Dis 68:1839–1842.

[28] Harrison BJ, Hutchinson CE, Adams J, Bruce IN, Herrick AL (2002) Assessing periarticular bone mineral density in patients with early psoriatic arthritis or rheumatoid arthritis. Ann Rheum Dis 61:1007–1011.

[29] Borman P, Babaoglu S, Gur G, Bingol S, Bodur H (2008) Bone mineral density and bone turnover in patients with psoriatic arthritis. Clin Rheumatol 27:443–447.

[30] Frediani B, Allegri A, Falsetti P, Storri L, Bisogno S, Baldi F et al (2001) Bone mineral density in patients with psoriatic arthritis. J Rheumatol 28:138–143.

[31] Dheda K, Cassim B, Patel N, Mody GM (2004) A comparison of bone mineral density in Indians with psoriatic polyarthritis and healthy Indian volunteers. Clin Rheumatol 23:89.

[32] Grisar J, Bernecker PM, Aringer M, Redlich K, Sedlak M, Wolozcszuk W et al (2002) Ankylosing spondylitis, psoriatic arthritis, and reactive arthritis show increased bone resorption, but differ with regard to bone formation. J Rheumatol 29:1430–1436.

[33] Nolla JM, Fiter J, Rozadilla A, Gomez-Vaquero C, Mateo L, Rodriguez-Moreno J et al (1999) Bone mineral density in patients with peripheral psoriatic arthritis. Rev Rhum Engl Ed 66:457–461.

[34] Grigoryan M, Guermazi A, Roemer FW, Delmas PD, Genant HK (2003) Recognizing and reporting osteoporotic vertebral fractures. Eur Spine J 12(Suppl 2):S104–S112.

[35] Papaioannou A, Kennedy CC, Ioannidis G, Gao Y, Sawka AM, Goltzman D et al (2008) The osteoporosis care gap in men with fragility fractures: the Canadian Multicentre Osteoporosis Study. Osteoporos Int 19:581–587.

[36] Geusens P, Vosse D, van der Linden S (2007) Osteoporosis and vertebral fractures in ankylosing spondylitis. Curr Opin Rheumatol 19:335–339.

[37] Lentle BC, Brown JP, Khan A, Leslie WD, Levesque J, Lyons DJ et al (2007) Recognizing and reporting vertebral fractures: reducing the risk of future osteoporotic fractures. Can Assoc Radiol J 58:27–36.

[38] Naves M, Diaz-Lopez JB, Gomez C, Rodriguez-Rebollar A, Rodriguez-Garcia M, Cannata-Andia JB (2003) The effect of vertebral fracture as a risk factor for osteoporotic fracture and mortality in a Spanish population. Osteoporos Int 14:520–5524.

[39] Black DM, Arden NK, Palermo L, Pearson J, Cummings SR (1999) Prevalent vertebral deformities predict hip fractures and new vertebral deformities but not wrist fractures. Study of Osteoporotic Fractures Research Group. J Bone Miner Res 14:821–828.

[40] Hasserius R, Karlsson MK, Nilsson BE, Redlund-Johnell I, Johnell O (2003) Prevalent vertebral deformities predict increased mortality and increased fracture rate in both men and

women: a 10-year population-based study of 598 individuals from the Swedish cohort in the European Vertebral Osteoporosis Study. Osteoporos Int 14:61–68.

[41] Lindsay R, Silverman SL, Cooper C, Hanley DA, Barton I, Broy SB et al (2001) Risk of new vertebral fracture in the year following a fracture. JAMA 285:320–323.