Clinical Vertebral Fractures in Patients with Ankylosing Spondylitis

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ABSTRACT. ***Objective.*** To evaluate the prevalence and characteristics of clinically confirmed vertebral fractures (CVF) in patients with ankylosing spondylitis (AS).

Methods. Coordinated by the Ankylosing Spondylitis International Federation in Germany and in Denmark, a self-administered questionnaire was sent to all their members about age, diagnosis, disease duration, HLA-B27 status, and history of CVF. Patients who were aware of having had a CVF were asked to return the questionnaire with additional specification of the location of CVF, associated trauma, neurological complications, therapy for these complications, and recovery. We also reviewed available radiographs.

Results. Out of 15,097 questionnaires, 59 patients (0.4%) reporting 66 CVF returned the complete questionnaire (46 men, 13 women). Mean age at fracture was 50 ± 9 years, after a mean duration of symptoms of 26 ± 11 years. CVF with wedging or crush or transverse fracture were reported in the cervical (n = 21, 36%), thoracic (n = 21, 36%), and lumbar spine (n = 16, 27%), with one unspecified. In 37 fractures (56%), patients reported no/low or medium trauma in relation to the fracture. In 31 fractures (47%), patients reported neurological complications, occurring mostly without trauma (n = 11, 35%) or after minimal trauma (n = 7, 23%). Twenty (65%) of these patients did not have full neurological recovery.

Conclusion. We found that 0.4% of patients with AS reported CVF at a mean age of 50 years, occurring after 2 decades of disease, mainly without trauma or after minimal trauma, with frequent neurological complications mostly followed by incomplete neurological recovery. (J Rheumatol 2004;31:1981–5)

Key Indexing Terms:
ANKYLOSING SPONDYLITIS
CLINICAL VERTEBRAL FRACTURES
OSTEOPOROSIS
NEUROLOGICAL COMPLICATIONS

Ankylosing spondylitis (AS) is a chronic inflammatory disease mainly of the axial skeleton that is characterized by ossification of the spinal discs, joints, and ligaments. This may lead to progressive rigidity of the spine. AS has a prevalence of 0.1% to 1.4% in Caucasian populations, correlating with the frequency of HLA-B27[1,2]. AS is usually diagnosed in the second or third decade of life, with a predominance of males at a ratio of 3:1.

Bone loss may be associated with inflammatory diseases such as AS and rheumatoid arthritis[3]. The reported prevalence of osteoporosis in terms of low bone mineral density (BMD) in patients with AS varies from 19% to 62%[3,4]. This large variation may reflect the difficulties in assessing BMD in AS due to spurious increase of BMD by the progressive appearance of syndesmophytes and ossifications. On the other hand, in patients with advanced AS BMD in the femur neck is reduced, indicating osteoporosis due to an inflammatory process[5-7]. Bronson, *et al* demonstrated that lateral lumbar spine dual energy x-ray absorptiometry (DEXA) showed low trabecular BMD in the presence of elevated anteroposterior lumbar spine BMD[8]. An increased prevalence of axial low BMD has been reported even in mild and early forms of AS[6,9]. Lee, *et al* showed significant intravertebral bone loss in patients with early and late disease during a mean followup of 15 months using quantitative computerized tomography[10]. Reid, *et al* showed in a longitudinal study that men with AS (mean disease duration 12.1 yrs) had an annual total bone mass loss of 2.2%[11].

The risk of morphometric vertebral fractures is increased in AS[12]. Cooper, *et al* described a relative risk of 7.6 (95% confidence interval 4.3–12.6) among patients with AS[12]. Other studies indicate that wedging vertebral fractures contribute to hyperkyphosis[13,14]. The reported prevalence of CVF varies widely (between 10% and 17%), but has not been assessed in a systematic way[6,12,13,15-17]. In several

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studies a high prevalence (between 29% and 91%) of major neurological complications was reported after CVF[16-19].

These data indicate that low BMD and vertebral fractures are features of AS. Our objectives in this study were (1) to estimate the prevalence of self-reported CVF in a large group of patients with AS using a questionnaire; (2) to describe the clinical characteristics of patients and the location of CVF; (3) to determine the relationship to trauma; and (4) to describe the neurological complications and any recovery.

MATERIALS AND METHODS

In this study, a self-administered questionnaire was distributed via the Ankylosing Spondylitis International Federation (ASIF) to all members of the German and Danish Ankylosing Spondylitis Society (14,127 in Germany, 970 in Denmark) by insertion in their membership journals. Nevitt, *et al* described a good reliability of data about vertebral fractures when gathered via self-administered questionnaires[20]. Patients were asked to complete and return the questionnaire if they had a history of a CVF. The questionnaire contained general items concerning AS, such as patient's age, sex, time of diagnosis, and HLA-B27 status, and the question if the diagnosis of AS was confirmed by their physician, according to the modified New York criteria[21]. Further, patients were asked to answer questions concerning the location of CVF, their relation to trauma, neurological complications (paresthesia and/or muscle weakness), clinical recovery, and therapy of these complications. Based on the narrative description of the trauma by the patients, the degree of trauma was categorized as: (1) no or low-energy fracture (a fracture occurring without trauma or after minor trauma); (2) medium-energy fracture (a fracture occurring after a fall at the same level, squeezing or dropping medium-weight objects onto fingers or toes, etc.); and (3) high-energy trauma (a fracture occurring after a fall from one level down to another, car accidents). The location of the fractures was based on the patient's description. Finally, we asked the patients to send the radiographs of the fractured vertebrae for review. Vertebrae T4 to L5 were graded as normal, wedge, biconcave (diabolo), or crush deformed, as defined by Genant, *et al*[22]. A fracture was defined as ≥ 20% reduction in anterior, middle, and/or posterior height. A transverse fracture was defined as an intra- or intervertebral fracture with dislocation. The clinical records of the Danish patients were checked by one author (JE).

Statistical analysis. The demographic variables were organized using descriptive analysis. Correlation coefficients between categorical values were calculated with a Pearson chi-square test. The significance of percentage differences was tested by chi-square tests for 2-by-2 tables. SPSS version 11 was used for these analyses.

RESULTS

Fifty-nine patients out of 15,097 returned the questionnaire and reported 66 CVF. The minimal prevalence of reported CVF in AS is thus 0.4%.

Patients' demographic data are shown in Table 1. All responders had a diagnosis of AS according to the modified New York criteria[21]. The patient group consisted predominantly of men (78%) of whom 81% were HLA-B27 positive. Patients reported fractures at a mean age of 50 ± 9 years, after a mean duration of symptoms of 26 ± 11 years.

Table 1. Characteristics of 59 patients with AS.

Sex, % men	78
HLA-B27 positive, %	81
Age, mean yrs ± SD	57 ± 10
Age at diagnosis of AS, mean yrs ± SD	32 ± 9
Years since diagnosis of AS, mean yrs ± SD	25 ± 12
Age at fracture, mean yrs ± SD	50 ± 9
Duration of symptoms at fracture, mean yrs ± SD	18 ± 11

Twenty-seven (46%) patients sent radiographs of the fracture(s) that could be reviewed. The other radiographs could not be retrieved. Examples of transverse, wedge, and crush fractures in respectively the cervical, thoracic, and lumbar spine are shown in Figures 1–3.

Table 2 shows the associated trauma levels. Twenty-one fractures (32%) were reported with no or low-energy trauma in relation to the CVF, 16 fractures (24%) were reported to be associated with medium-energy trauma, and 22 fractures (33%) with high-energy trauma. In 7 fractures (11%), patients did not record the level of associated trauma.

We noted a statistically significant association between the fracture location and the morphology of the fracture (Table 3). All vertebral regions were reported: 21 fractures (36%) in the cervical spine, 21 (36%) in the thoracic spine, and 17 (26%) in the lumbar spine. One patient could not specify the fracture level. Crush fractures were seen mostly in the lower regions of the spine (n = 5), whereas transverse luxation only occurred in the cervical spine (chi-square = 15, p = 0.05).

Of the 66 CVF, 31 (47%) were associated with neurological complications, varying from transient paresthesia to sustained loss of strength in arms or legs. Only 11 fractures (35%) were reported with full recovery, either spontaneously or after intervention in 3, whereas in 20 fractures

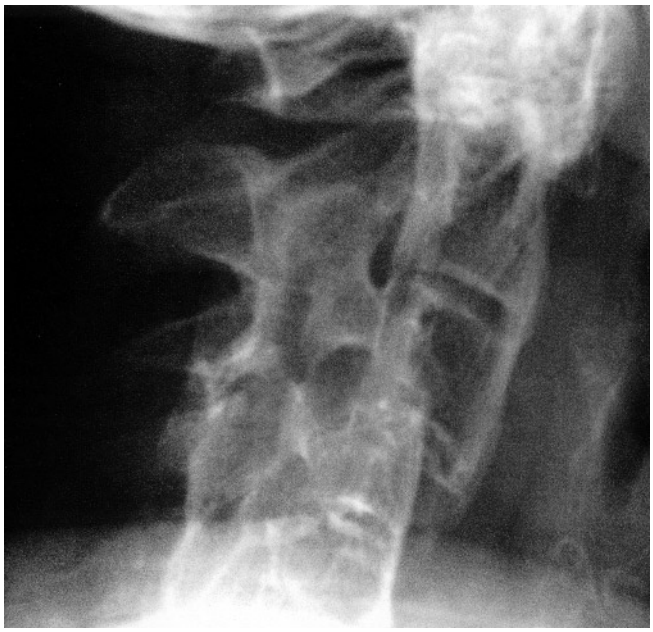

Figure 1. Radiograph of a transverse vertebral fracture in the cervical spine in a 53-year-old man with AS (disease duration of 16 yrs) after a fall from a scaffold, complicated by paralysis in both arms and legs and loss of sensation. The motor function recovered completely, the sensory loss only partially.

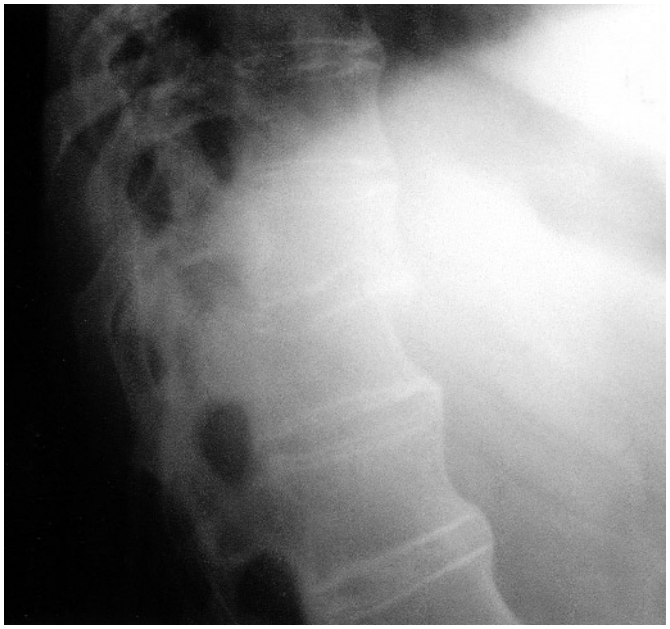

Figure 2. Radiograph of a wedge fracture in the thoracic spine in a 47-year-old man with AS (disease duration 7 yrs) after a fall at the same level, with no neurological complication.

(65%) patients experienced no or only partial recovery, sometimes in spite of surgical intervention that was performed (Table 4).

Neurological complaints were significantly associated with the morphology of the fracture. All luxation fractures were complicated by neurological features, crush fractures mostly were without neurological complications (chi-square = 11, $p < 0.05$). Neurological complications occurred more frequently in patients reporting no or low-energy trauma than in patients with high-energy trauma (chi-square = 7.7, $p < 0.05$).

The mean disease duration at the time of fracture after a no/low-energy trauma was 13.6 years compared to 20.4 years after a high-energy trauma ($p = 0.07$). No significant correlations were found between neurological complaints and location of fracture or sex.

DISCUSSION

Osteoporosis has only recently been recognized as a feature in AS[9]. This is associated with a significantly increased incidence of vertebral fractures in patients with AS, even after minor trauma. In contrast, Cooper, *et al* found that the fracture risk in the appendicular skeleton was not increased, indicating that osteoporosis in AS is confined to the spine[12]. We report here a minimal prevalence of CVF of 0.4% in patients with AS. These fractures occurred at a mean age of 50 years, after mean disease duration of 18 years. They occurred even after no or minimal trauma and were characterized by a high number of neurological complications (47%), with complete neurological recovery in only 35% of the cases.

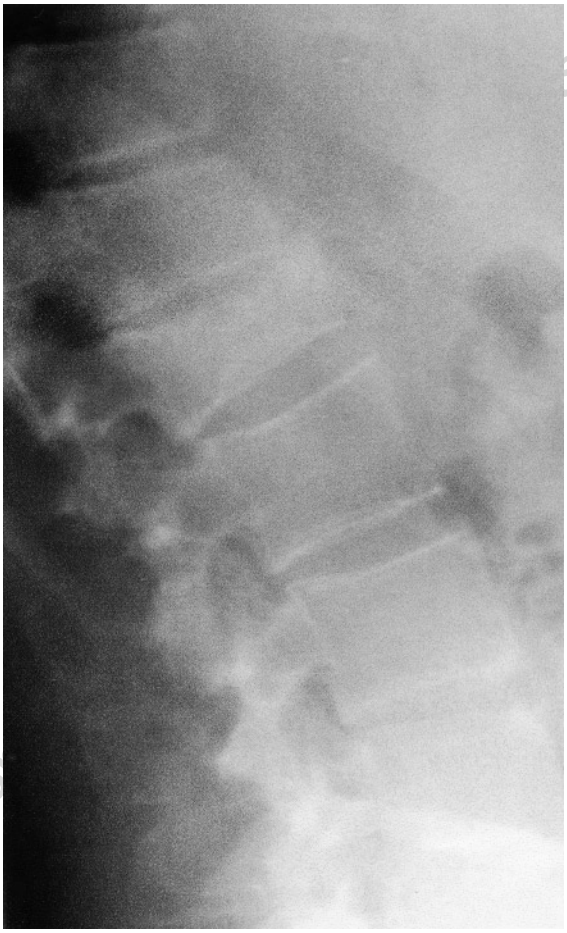

Figure 3. Radiograph of a crush fracture in the lumbar spine in a 42-year-old man with AS (disease duration 11 yrs) after stepping out of a car, followed by paralysis and loss of sensation in both legs. There was partial recovery of motor and sensory function.

Table 2. Energy level of trauma.

	No. of Fractures (%)
No/low energy	21 (32)
Medium energy	16 (24)
High energy	22 (33)
Unknown	7 (11)

Table 4. Neurological complaints and clinical outcome of fracture.

	Fractures, N (%)
Neurologic involvement	31/66 (47)
Sensory loss	11/31 (35)
Paralysis	6/31 (20)
Combination	14/31 (45)
Complete recovery	11/31 (35)

Table 3. Fracture site and morphometry of fractures.

Facture Site	No. of Patients (%)	No. of Fractures (%)	Morphometry of Fracture, No. Reviewed			
			Crush	Diabolo	Wedge	Luxation
Cervical spine	21 (37)	21 (32)	0	0	4	7
Thoracic spine T1–6	5 (8)	7 (11)	1	0	2	1
Thoracic spine T7–12	16 (27)	20 (30)	3	1	4	0
Lumbar spine	16 (27)	17 (26)	2	1	4	0
Unknown	1 (1)	1 (1)				

The minimal prevalence of 0.4% that we observed is lower than the figure reported by Hitchon, *et al*, who found 13 out of 266 patients with AS (5%) with clinical vertebral fractures[16]. Such a high percentage could, however, be due to a referral bias by preferential referral to a specialized clinic.

A wide range of prevalence of CVF in AS is reported in the literature (5% to 18%). This wide variation could be due to patient selection, differences in the definition of vertebral fracture, or differences among centers[6,12,13,15-17].

Our study design had a number of limitations. Only patients who had suffered clinically from fractures were asked to respond. Overall, about one-third of all fractures come to clinical attention[23]. This low rate of diagnosis may also be related to mildness of symptoms or the absence of acute pain. Particularly in patients with AS, who suffer from back pain continuously, worsening of complaints may easily be (mis)interpreted as disease flare or muscle strain. Therefore, probably only more severe cases have been reported in our survey. The milder cases could have been missed or forgotten. Furthermore, patients may not have responded to our questionnaire because they did not read the newsletter. Therefore our figure represents really the minimal prevalence of CVF in AS.

Interestingly, we identified a high percentage of patients with CVF in the cervical spine and patients with transverse vertebral fractures, features that are not reported in primary osteoporosis[24]. A possible explanation is that, due to the rigidity of the spine in AS, less shock absorption is possible, which makes the bony spine more prone to transverse vertebral fractures. The finding that CVF in the cervical spine do occur in AS patients is confirmed by others[13,17-19]. The mean age at time of fracture was 50 ± 9 years, after a mean of 2 decades of disease. This is in accord with reports that describe fractures occurring in the third decade after the disease has been diagnosed[6,15,19]. Thus CVF in AS occur at a much earlier age compared to primary osteoporosis, indicating that AS is a risk factor for CVF, as has also been shown for morphometric vertebral fractures[12].

Only a minority of patients reported an adequate trauma before the CVF, a finding confirmed by others[16-19]. Forty-seven percent of fractures were reported to be associated with neurological complications in our study. Only 35% of patients reported full recovery. We focused in particular on paresthesia and muscle weakness, as pain is a frequent and almost normal symptom in AS. Data on neurological complications are scarce in the literature[16-19,25,26]. However, several investigators report a high prevalence for such manifestations. Hunter, *et al*[17] report 22 spinal fractures in 20 patients with neurological complaints, varying from no associated deficit to death by complete spinal cord lesion. Fox, *et al*[18] describe a retrospective review from the Mayo Clinic in which they identified 33 patients with AS in a period of 5 years who underwent surgery 41 times for spinal fractures. Presurgical neurological deficits were recorded in 13 patients, resulting from several causes and of varying severity. Nguyen, *et al*[26] report 10 cases of neurological complications after vertebral fractures due to postmenopausal osteoporosis over a period of 4 years. In their literature survey they found a total of only 71 case reports. These figures suggest that the prevalence of neurological complications is much lower in this widespread osteoporotic condition.

Neurological complications occurred significantly more after minimal or no trauma than after adequate trauma. This suggests that no or low-energy trauma fractures occurred in patients with the most severe degree of osteoporosis. One can hypothesize that a low BMD in combination with a reduced capacity for shock absorption makes the already rigid spine prone to developing complicated fractures. Further, CVF after low-energy or no trauma occurred at a younger age than CVF with high-energy trauma. A possible explanation could be that these patients had high disease activity and were therefore more prone to early bone loss and fractures.

Another limitation of this study is that these cases are not representative of the whole population of AS patients due to response bias. However, the frequency and severity of the complications warrant further research. Indeed, assuming that this patient group had the most dramatic clinical picture, further studies are necessary to evaluate the clinical significance of the increased risk for vertebral fractures in AS, in order to promptly diagnose and effectively treat patients at risk.

We describe 59 patients with AS, who reported 66 clinically confirmed vertebral fractures at a mean age of 50

years, notably early in the disease, mainly without trauma or after minimal trauma, with frequent neurological complications mostly followed by incomplete neurological recovery.

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