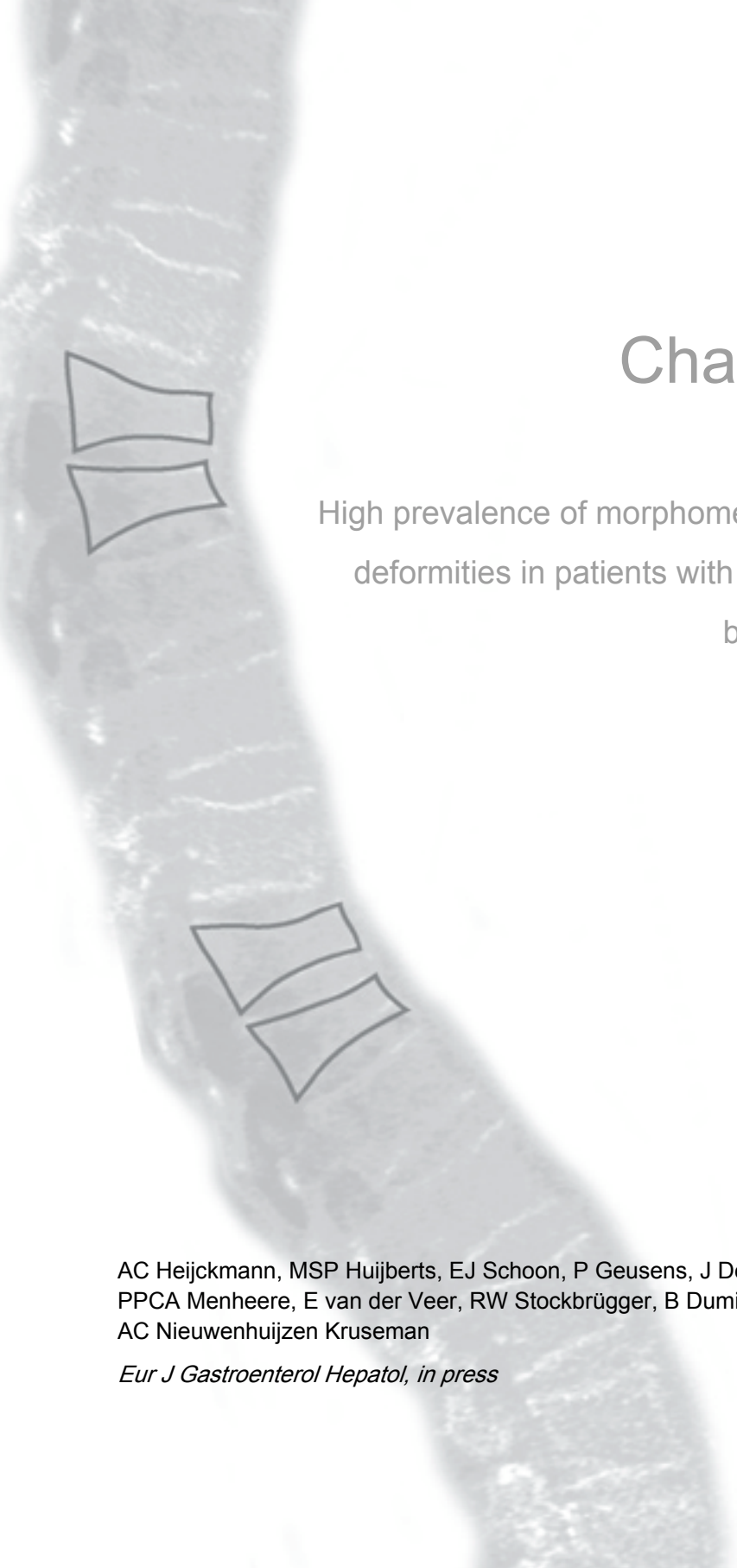

Chapter 4

High prevalence of morphometric vertebral deformities in patients with inflammatory bowel disease

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Abstract

Background
Previous studies have documented that the prevalence of decreased bone mineral density (BMD) is elevated in patients with inflammatory bowel disease (IBD). The objective of the current study was to investigate the prevalence of vertebral deformities in IBD patients and their relation with BMD and bone turnover.

Methods
109 Patients with Crohn's disease (CD) and 72 with ulcerative colitis (UC) (age 44.5±14.2 year) were studied. BMD of the hip (by dual-energy X-ray absorptiometry (DXA)) was measured and a lateral single energy densitometry of the spine for assessment of vertebral deformities was performed. Serum markers of bone resorption (ICTP) and formation (PINP) were measured and determinants of prevalent vertebral deformities were assessed using logistic regression analysis.

Results
Vertebral deformities were found in 25% of both CD and UC patients. Comparing patients with and without vertebral deformities, no significant difference was found between Z- and T-scores of BMD, or levels of ICTP and PINP. Using logistic regression analysis the only determinant of any morphometric vertebral deformity was gender. The presence of multiple vertebral deformities was associated with older age and glucocorticoid use.

Conclusions
The prevalence of morphometric vertebral deformities is high in CD and UC. Male gender, but neither disease activity, bone turnover markers, clinical risk factors, nor BMD predicted their presence. The determinants for having more than one vertebral deformity were age and glucocorticoid use. This implies that in addition to screening for low BMD, morphometric assessment of vertebral deformities is warranted in CD and UC.

Introduction

Decreased bone mineral density (BMD) is a frequent finding in inflammatory bowel disease (IBD). Z-scores <-1.0 can be found in 32 to 38% of patients with Crohn's disease (CD) and in about 25% of patients with ulcerative colitis (UC).[1] An even higher prevalence of decreased bone mass can be found when a T-score is used to express BMD. Following this approach, we found in a previous study osteopenia and osteoporosis in respectively 45 and 13% of patients with CD.[2]

Specific disease-related factors contributing to decreased BMD in IBD patients involve inflammatory cytokines with associated increased bone resorption, malabsorption due to disease activity or extensive intestinal resection, glucocorticoid (GC) use, inability to achieve peak bone mass when the disease starts in childhood, malnutrition and hypogonadism induced by the chronic inflammatory condition, and eventually superposed on other clinical risk factors such as history of fracture, family history of fractures, immobilization, low BMI, smoking and alcohol abuse.[1-7]

As a result of the decreased BMD and disease related factors an increased overall fracture risk can be expected in patients with IBD.[1] In a population-based cohort study of patients with IBD the incidence rate ratio was 1.4 (95% confidence interval (CI): 1.3-1.6) for spine, hip, rib and forearm fractures compared to controls, 1.7 (CI: 1.3-2.2) for clinical vertebral fractures and 1.6 (CI:1.3-2.0) for hip fractures with similar increases for CD and UC.[8] In a primary care-based case-control study similar increases in the risk of clinical vertebral and hip fractures were found in patients with IBD.[9] In a large Danish case-control study a 2.5-fold increase in the risk of symptomatic low energy fractures of spine, feet and toes was found among women with CD, but not in men or patients with UC.[10] In a recent extensive review, Bernstein and Leslie concluded that patients with IBD have a moderate increased risk of clinical fractures but mentioned a lack of studies on the presence of morphometric vertebral fractures and the absence of data in UC.[11]

Indeed, the majority of studies on fractures in IBD concern clinical fractures. In particular vertebral fractures are however often not clinically recognized and can accumulate silently.[12] It is well established that a vertebral fracture, clinical or morphometric only, is a strong risk factor for subsequent osteoporotic fractures, not only at the spine but also at other sites and regardless of BMD.[13-16] Furthermore, vertebral fracture risk is related to the number and severity of prevalent vertebral fractures, while the risk of non-vertebral fractures is related to the severity of prevalent morphometric vertebral fractures.[16,17]

Data on the prevalence of morphometric vertebral fractures in subjects with IBD are scarce. A prevalence of 22% was found on X-rays using a decrease in anterior, mid or posterior height of >20 % in a study with 156 patients with CD

and osteopenia or osteoporosis, ranging from 20% in patients <20 years old to 50% in patients older than 60 years.[18] In another study a prevalence of morphometric vertebral fractures on X-rays (any height loss of >20%) of 14% was found (11% in patients <30 years up to 31% in patients older than 60 years), with no correlation with bone mineral density and use of glucocorticoids.[19] The prevalence of morphometric vertebral fractures in UC is not known.
For these reasons we investigated in a cohort of 181 subjects with IBD, including CD as well as UC patients, the prevalence of morphometric vertebral deformities. The findings were related to BMD, bone turnover parameters and clinical risk factors to get an impression about the risk of vertebral fractures in IBD patients and to what extent this is related to differences in BMD and bone turnover.

Patients and methods

Patients

Between January 2002 and July 2003, all patients with inflammatory bowel disease who had a disease duration of at least one year, and attended the outpatient clinic of the University Hospital Maastricht, were asked to participate in this cross-sectional study. Two hundred and two patients (78%) agreed. All patients were Caucasians and diagnosed with CD or UC on clinical grounds using endoscopic and/or radiological evidence, and by histological investigation of mucosal biopsies and/or surgical specimens when available. For confirmation of the CD diagnosis the Lennard-Jones criteria[20] and for UC the Truelove and Witts criteria[21] were applied. Sixteen patients with known causes of bone mass abnormalities, such as renal failure, thyroid dysfunction, alcoholism and ankylosing spondylitis were excluded. None of the other patients had any significant co-morbidity. Five patients were excluded because of incomplete data. Thus 181 patients were included in this study. This group consisted of 81 pre-menopausal women, 26 post-menopausal women, and 74 men. Demographic, clinical and treatment data of these patients are summarized in Table 4.1. The clinical records of all patients were reviewed. Age of onset of CD and UC, disease duration and medication use were derived from the medical records. Glucocorticoid (GC) use was scored as never, previous (stopped more than three months before including in the study) or current. If patients were currently using glucocorticoids (GCs) the daily dose was noted. Furthermore, current use of other immunosuppressive medication, vitamin D and calcium or budenoside use were also recorded.

Table 4.1 Demographic, clinical, and treatment variables in the study patients (n=181).

Variable	All n=181	Crohn's disease n=109 (60%)	Ulcerative colitis n=72 (40%)	p* between CD and CU
Demographic variables				
Female sex	107 (59)	75 (69)	32 (44)	0.001
Postmenopausal	26 (14)	17 (16)	9 (13)	ns
Age (years)	44.5 ± 14.2	41.9 ± 13.9	48.5 ± 13.8	<0.01
Body mass index (kg/m^2)	25.0 ± 4.2	24.3 ± 4.0	26.0 ± 4.4	0.01
Daily dietary calcium intake (mg)	687 ± 360	663 ± 369	723 ± 347	ns
Clinical variables				
Disease duration (years)	8 (1-36)	8 (1-36)	9 (1-28)	ns
1,25$(OH)_2D_3$ (nmol/l)	0.13 ± 0.04	0.13 ± 0.04	0.13 ± 0.04	ns
CDAI (>150=active disease)		118 ± 88		
CAI (score 0-21)			5.9 ± 3.5	
Physical activity index (score 0-18)	8.8 ± 3.6	8.8 ± 3.6	8.7 ± 3.8	ns
Treatment variables				
GC use never	40 (22)	19 (17)	21 (29)	ns
GC use ever	119 (66)	81 (74)	38 (53)	<0.01
GC use current	22 (12)	9 (8)	13 (18)	ns
Current use of bisphosphonates	22 (12)	14 (13)	8 (11)	ns
Current calcium supplement	56 (31)	44 (40)	12 (17)	0.001
Current vitamin D supplement	53 (29)	41 (38)	12 (17)	<0.01
Current use of immunosuppressive medication	84 (46)	64 (59)	20 (28)	<0.001
Current use of budenoside	54 (30)	46 (42)	8 (11)	<0.001
Daily dose GC current group (mg)	6,25 (0-30)	5 (0-30)	10 (0-20)	ns
Clinical risk factors for osteoporosis				
Fracture >50 years	0	0	0	
Vertebral deformity by DXA	45 (25)	25 (23)	20 (28)	ns
Low body weight (<60 kg)	30 (17)	22 (20)	8 (11)	ns
Low physical activity index ≤5	37 (21)	20 (19)	17 (24)	ns
Mother with hip deformity	11 (6)	5 (5)	6 (8)	ns

Data are given as mean ± SD, median (range) or number (%) Reference parameters: 1,25(OH)2D3 0.040-0.200 nmol/l; Abbreviations: 1,25(OH)2D3, 1,25 dihydroxyvitamin D; CDAI, Crohn's disease activity index; CAI, colitis activity index; GC, glucocorticoid; DXA, dual X-ray absorptiometry

Patients were evaluated according to a standard protocol that included measurement of height and weight, measurement of bone mineral density (BMD) and collection of a blood sample and morning urine.

Calcium intake of all patients was scored on the basis of a detailed dietary list. Known clinical risk factors for osteoporosis (weight below 60 kg, hip fracture in the mother, history of fractures after age 50, menopausal status and severe immobilization) as well as daily activities and exercise were assessed by a validated questionnaire,[22] in which sports, daily and work activities are scored with a minimum of zero and a maximum of eighteen. Current disease activity in CD was evaluated using the Crohn's Disease activity Index (CDAI)[23] and in UC the colitis activity index (CAI)[24] was applied. Patients with CD were considered to have active disease when CDAI was >150. Informed consent was obtained

from all participants and this study was approved by the ethical committee of the hospital.

Laboratory assays

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 (interassay coefficient of variation (IE-CV) 3.2%, intra-assay CV (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). The Z-score for these bone markers was 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.[25] Serum 1,25-dihydroxy-vitamin D concentration was determined by RIA using a commercially available kit (IDS Ltd, Boldon, England, IE-CV 18%, IA-CV 15%).

Bone Mineral Density and morphometry

In all 181 patients bone mineral density (BMD) of the hip was measured by dual X-ray absorptiometry (DXA, Hologic QDR 4500). As reference group the NHANES III database was used. Measurements were done in the standard projection, and results were reported for femoral neck and trochanter. Standard procedures supplied by the manufacturer for scanning and analyses were performed. Calibration with the manufacturer's spine phantom and quality control analysis were performed daily. The coefficient of variation for BMD measurements was 1.0%. The number of patients with osteopenia and osteoporosis was determined according to the WHO classification in which osteopenia is defined as a T-score between -1 and -2.5 and osteoporosis as a T-score ≤-2.5. To adjust for age and gender, Z-scores were used.
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)).[26] The scans obtained were analyzed twice by one trained operator (intra-observer correlation: 0.85), using the semi-quantitative method of Genant.[27] 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 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.[27] For crush deformity ratio was calculated by dividing Hp of the vertebra with Hp of the vertebra below. Grade 1 (mild) deformity was defined

as a reduction of 20 to 25% in any height, grade 2 (moderate) 25 to 40% and grade 3 more than 40% (severe).

Statistics

Student *t*-tests, chi-square tests, and one-way ANOVAs were used, depending on the variables and subgroups tested. The analyses were performed with Z-scores in order to correct for age and gender when comparing (sub)groups. One-sample *t*-tests were used to compare patient scores with norm scores. A logistic regression analysis was performed to examine the determinants of morphometric vertebral deformities. Sex, age, weight, disease, illness duration, CDAI, CAI, physical activity, vitamin D, GC use, current use of vitamin D, calcium, immunosuppressive medication, budenoside and hip fracture mother were examined as potential determinants. Furthermore, we analysed the risk factors for having >1 vertebral deformity.

Results

Bone mineral density

The results of BMD measurements and bone turnover markers are shown in Table 4.2. In the total group, osteoporosis was found in 4% of patients and osteopenia in 55%. Excluding patients currently using glucocorticoids and/or bisphosphonates, the average Z-score of the femoral neck (FN) was decreased compared to the reference population (-0.29, CI: -0.45, -0.14; p<0.001). The average Z-scores were lower in patients with CD (trochanter:-0.27, CI: -0.45, -0.08 and FN: -0.51, CI: -0.70, -0.33) compared with patients with UC (trochanter 0.27, CI: 0.00, 0.53 and FN: 0.06, CI: -0.19, 0.31; p=0.001 and <0.001, respectively).

Table 4.2 BMD variables and bone turnover markers in IBD patients currently not using bisphosphonates and/or glucocorticoids.

Variable	Total group	Crohn's disease	Ulcerative colitis	p between CD and CU
	n=143	n=88	n=55	
Z-score				
Femoral neck	-0.29 ± 0.94*	-0.51 ± 0.89*	0.06 ± 0.93	<0.001
Trochanter	-0.06 ± 0.94	-0.27 ± 0.86*	0.27 ± 0.98	0.001
Bone markers in serum				
ICTP (µg/l)	3.6 ± 1.3	3.7 ± 1.3	3.5 ± 1.2	ns
Z-score ICTP	0.49 ± 1.6*	0.53 ± 1.3*	0.41 ± 1.6	ns
PINP (µg/l)	48.7 ± 27.5	50.9 ± 26.0	45.1 ± 29.8	ns
Z-score PINP	0.59 ± 1.6*	0.69 ± 1.6*	0.42 ± 1.7	ns

Data are given as mean ± SD; * p<0.05 versus 0 for Z-scores; Abbreviations: ICTP, carboxy-terminal cross-linked telopeptide of type I collagen; PINP, procollagen type I amino-terminal propeptide.

Patients who never used glucocorticoids (n=40) had normal Z-scores of FN and trochanter compared with patients with previous or current use of this medication who had lower BMD values (respectively: -0.07, CI: -0.35, 0.22 versus -0.52, CI:-0.68, -0.37; p<0.01 and 0.17, CI: -0.08, 0.42 versus -0.31, CI: -0.47, -0.15; p<0.01).

Bone turnover parameters

In the total group of patients currently not on bisphosphonates and/or glucocorticoids the average Z-score for ICTP (Z-ICTP) was increased compared with the reference population (0.49, CI: 0.22, 0.76; p<0.001), as well as the marker of bone formation (Z-PINP) (0.59, CI: 0.31, 0.86; p<0.001). This was especially observed in patients with CD (Z-ICTP: 0.53, CI: 0.19, 0.88; p<0.01, and Z-PINP: 0.69, CI: 0.36, 1.03; p<0.001 respectively).

Morphometric vertebral deformities

Vertebral deformities (ratio of <0.80) were found in 77 vertebrae of 45 patients (25% of total group). This prevalence was similar in both subgroups of patients. Fifty-nine of the deformities were wedge deformities, 16 biconcave and two crush deformities. Fifty one were mildly deformed, 22 moderate and four severe deformations were seen. With regard to the localization of the deformities (Table 4.3), prevalence peaks were found in the low thoracic region. Seventeen patients (age 51.5±17.0 years) had more than one vertebral deformity. This group consisted of eleven men, three premenopausal and three postmenopausal women. The majority of these patients (82%) was current or previous glucocorticoid user. Comparing the groups with and without vertebral deformities, no significant difference was found between Z- or T-scores of BMD of the trochanter or femoral neck, nor in Z-ICTP, or Z-PINP (Table 4.4, Figure 4.1). The two differences between these groups were an older age (p<0.05) and more males (p<0.01) in the group with deformities. Furthermore, no differences were seen between the two subgroups in current use of calcium and/or vitamin D supplements, aminosalicylates, immunosuppressive medication and budenoside. Logistic regression analysis revealed that the only determinant of prevalent morphometric vertebral deformity was sex (OR: 2.25, p<0.05, CI: 1.11, 4.54), indicating that men have a more than twofold higher chance of morphometric vertebral deformity. In addition, the only determinants for having more than one vertebral deformity were age (OR: 1.05, p=0.02, CI: 1.05-1.09) and current GC use (OR: 4.98, p=0.01, CI: 1.42, 17.49).

Table 4.3 Distribution of the number of vertebral deformities and rating of their severity.

	Number of deformities	Mild deformity	Moderate deformity	Severe deformity
T4				
T5				
T6	5	3	2	
T7	1	1		
T8	4	2	2	
T9	6	5	1	
T10	7	5	2	
T11	23	15	7	1
T12	19	12	5	2
L1	5	4	1	
L2	3	1	1	1
L3	2	1	1	
L4	2	2		
L5				

Table 4.4 Patients with morphometric vertebral deformity (n=45) versus without morphometric vertebral deformity (n=136).

Variable	Without vertebral deformity	With vertebral deformity	p*
Z-score			
Femoral neck	-0.40 ± 0.96	-0.49 ± 0.93	ns
Trochanter	-0.19 ± 1.01	-0.27 ± 0.75	ns
T-score			
Femoral neck	-0.95 ± 0.91	-1.22 ± 0.88	ns
Trochanter	-0.45 ± 0.96	-0.63 ± 0.78	ns
Bone markers in serum			
Z-score ICTP	0.58 ± 1.8	0.75 ± 1.8	ns
Z-score PINP	0.72 ± 2.4	0.34 ± 1.6	ns
Demographic and patient variables			
Males	48 (35)	26 (58)	<0.01
Postmenopausal women	19 (14)	7 (16)	ns
Crohn's disease/Ulcerative colitis	84/52	25/20	ns
GC use, never	30 (22)	10 (22)	ns
GC use, previous	90 (66)	29 (65)	ns
GC use, current	16 (12)	6 (13)	ns
Disease duration (years)	8 (1-36)	8 (1-34)	ns
Age (years)	43.3 ± 13.6	48.2 ± 15.2	<0.05
Body mass index (kg/m^2)	24.9 ± 4.4	25.3 ± 3.8	ns
CDAI (>150=active disease)	120 ± 89	110 ± 84	ns
CAI (score 0-21)	5.9 ± 3.3	5.9 ± 4.0	ns
Physical activity index (score 0-18)	8.6 ± 3.6	9.3 ± 3.8	ns
Calcium intake (mg)	691 ± 366	674 ± 345	ns

Data are given as mean ± SD, median (range) or number (%). * p between patients with and without vertebral deformity; Abbreviations: ICTP, carboxy-terminal cross-linked telopeptide of type I collagen; PINP, procollagen type I amino-terminal propeptide; GC, glucocorticoid; CDAI, Crohn's disease activity index; CAI, colitis activity index.

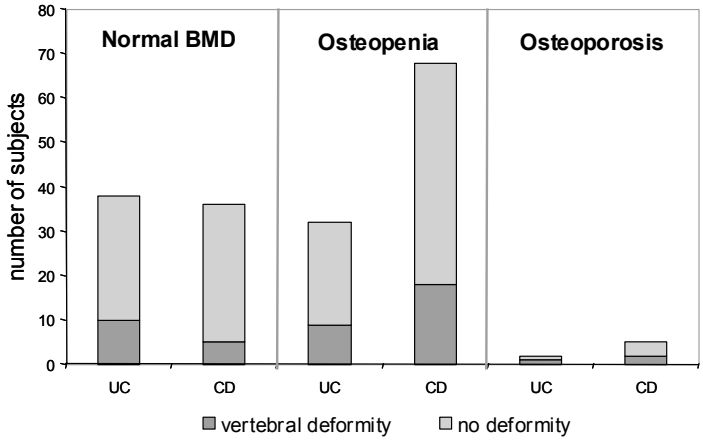

Figure 4.1 Number of patients with and without a vertebral deformity.
Abbreviations: UC, ulcerative colitis; CD, Crohn's disease

Discussion

In our series of patients with IBD we found vertebral deformities with quantitative morphometric X-ray absorptiometry (MXA) in 25% of patients. This high prevalence is remarkable as the majority of our patients was relatively young and premenopausal.

Our observations of an increased prevalence of morphometric vertebral deformities are in line with the few clinical studies reported on vertebral deformities in CD. Stockbrügger and co-workers found on X-rays a prevalence of 14% in a younger population with CD and this increased to 43% in female patients above 60 years.[19] In another study in 156 patients with CD and osteopenia and osteoporosis, a prevalence of 22% of vertebral deformities was found.[28] Other studies also revealed an increased risk for clinical vertebral fractures in both CD and UC.[8,9,29] Our finding of a preferential localization of vertebral fractures at the mid and lower thoracic spine is also in line with earlier findings.[19] In addition, an increase of morphometric vertebral deformities similar to CD was found in UC, which has not been reported in the literature before.

To what extent the high prevalence of vertebral deformities in IBD differs from subjects without IBD is uncertain, as no data on non-clinical deformities in healthy young and premenopausal individuals are available. The best comparison with healthy subjects for the present study stems from the EVOS study, in which in a very large cross-sectional population based study European subjects aged 50 to 79 years were investigated. The prevalence of vertebral deformities on X-rays in this study was 12% (range 6-21%) in males

and females.[30] The Rotterdam study, in which 3469 men and women aged 55 years and older were studied, revealed a prevalence of vertebral deformity suggestive of fracture in 6.9% of men and 7.5% of women.[31] In a previous study on 60 subjects (mean age 49±13 years), who were followed after initial successful treatment for differentiated thyroid carcinoma, we found vertebral deformities in 7%.[32] All these data support the fact that IBD is a relevant risk factor for vertebral deformity suggestive for fracture.

For the determination of vertebral fractures a variety of morphometric approaches can be used. These different approaches can result in slightly different outcomes.[27,33-35] Compared with subjective qualitative assessment, quantitative morphometry is a more reproducible method for assessing vertebral deformity and therefore these approaches are often used in conjunction. As, however, a gold standard for vertebral fracture is not available, it is still not clear which method is the most appropriate to establish vertebral deformities and on the basis of that to determine the occurrence of vertebral fractures. We followed the method of Genant,[27] which is based on a reduction of the ratios of anterior, middle or posterior heights. This is the simplest and most practical method.[36] It is also the method used in the majority of studies on IBD patients published[18] and an association with future fracture risk is documented.[37] 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.[35] Relative to the method of Genant, the method of Eastell may result in a lower prevalence of vertebral deformities. In our series, use of the method of Eastell resulted in vertebral deformities in 20% of patients (data not shown), which is indeed lower than the prevalence found after the method of Genant, but still indicates a substantial prevalence in this young population.

We used MXA instead of standard spine radiographs for morphometric determination of vertebral deformities. Several studies have documented that MXA is comparable to standard spine radiographs for this approach.[38-41] MXA, also called VFA (vertebral fracture assessment with DXA), has several advantages over vertebral morphometry on conventional spinal radiographs (MRX). The radiation dose is much lower (<80μSv) and assessment of BMD and vertebral deformities can be combined. Although MXA is thus an established technology to detect vertebral fractures and to identify patients likely to benefit from pharmacological therapy who otherwise might not be treated,[42] this technology has some limitations as well. These include limited ability to provide a differential diagnosis for the detected deformities, lower sensitivity for milder fractures and inability to evaluate the uppermost thoracic levels. However, its negative predictive value is high.[17] Other disorders that may cause changes in vertebral shape involve congenital abnormalities and conditions as severe osteoarthritis[43] and Scheuermann's disease. We have,

however, no indications that these relatively rare conditions may have interfered with our observations. On the other hand, vertebrae in the mid-thoracic spine and thoraco-lumbar junction are slightly more wedged than in other regions of the spine[34,44] and, as a result, normal variations may be misinterpreted as mild vertebral deformities.[45,46] This may have contributed to overestimation of vertebral deformities in our series, although we feel only to a limited extent.

The occurrence of vertebral deformities in our series was equally distributed between subjects with a normal and osteopenic BMD at the hip. Only a few subjects had osteoporosis according to the WHO criteria, even when patients on bisphosphonates were included. BMD of patients with vertebral deformities was not different from the other patients studied. These findings are in line with other studies.[19] In one of these studies, bone mass and fracture risk was determined and revealed a reduced BMD of the lumbar spine in patients with vertebral fractures compared with those without (T-score -2.50±0.88 versus -2.07±0.66; $p<0.05$), but also no relevant differences of BMD at the hip.[18] This is in line with the many observations that indicate that low BMD is only one of the components that determines fracture risk and that most fractures,[47] whether clinical or morphometric, occur in patients without osteoporosis in terms of a T-score $\leq$-2.5.[47] Therefore, our results support the current trend towards identifying patients at risk for fracture even when BMD is normal[7] as reflected in the current WHO initiative to develop refined models for fracture prediction in the individual patient.[47] The clinical consequence of our findings is that a more systematic search for vertebral deformities is warranted in CD and UC, as suggested by others.[11]

It is well known that chronic inflammatory diseases affect bone physiology by the production of cytokines[48,49] such as interleukin-6 and 17, tumour necrosis factor, the RANKL/OPG balance and the Wnt signalling pathway, probably mainly by an influence on bone turnover.[50-52] We indeed found an increase in bone turnover parameters in both groups of patients, which was more pronounced in CD than in UC. In postmenopausal women, the level of bone turnover has been shown to be as strong a predictor of fractures as the level of BMD and independent of low BMD.[53,54] This may be due to an effect of increased bone turnover on bone microarchitecture, in particular a loss of horizontal trabeculae not reflected in a change of BMD but nevertheless associated with an increased bone fragility and thus fracture risk. This may imply that changes in microarchitecture of bone rather than changes in BMD are involved in the occurrence of vertebral deformities in IBD and that vertebral deformities are therefore a better reflection of bone failure than low BMD. An alternative explanation may be that vertebral deformities in IBD occur during phases of active disease and increased bone turnover and bone loss, with subsequent recovery of bone during improvement of the IBD condition

obscuring the relation of BMD with fracture. This is however unlikely, as we found no relation between vertebral deformities and current disease activity.
In our study, male gender was a determinant for having a vertebral deformity. In a previous study were men with CD at greatest risk for osteoporosis,[55] but no gender difference was shown in studies on fracture risk. Age was the determinant for having more than one vertebral deformity as it is a determinant in most epidemiological studies on fracture risk in healthy subjects.[56,57] This was also found in a study of 218 patients with CD in which follow-up data at 20 years were compared with those of age- and gender matched controls. An overall risk ratio of 2.2 for a thoraco-lumbar fracture was calculated in this study with IBD and age as the only determinant and not use of glucocorticoids or intestinal resections.[58] In another study, GC use per se appeared also not to be an important risk factor for fractures in IBD, although this study showed an increased fracture risk in CD but not in UC after long term use of GCs.[10] We found that patients with current use of glucocorticoids had a higher prevalence of multiple (>1) vertebral deformities. This is in line with the view that long term use of GCs is an independent risk factor for fracture.[59]
Limitations of our study are the cross-sectional design and the lack of an age and sex matched control population. Another limitation is the measurement of BMD in the hip only. This may have been contributed to an underestimation of osteopenia as it can not be excluded that more influence of BMD on risk of non-clinical vertebral fractures would have been found if DXA of the spine was also performed. However, as measurement of the hip allows measurement of both trabecular and cortical bone, a recent study shows that for this reason hip measurements may be superior to the spine in overall fracture prediction.[60]
In conclusion, we performed a large cross-sectional outpatient-based study on patients with Crohn's disease and ulcerative colitis and have demonstrated that in patients with these conditions the prevalence of non-clinical vertebral deformities suggestive of vertebral fractures is substantial, even in patients with normal BMD. Disease activity, glucocorticoid therapy and known risk factors for fracture appear to be poor predictors for the occurrence of these asymptomatic vertebral deformities, although GC use predicted the presence of multiple deformities. This implies that in addition to screening for osteoporosis by means of a bone mineral density measurement, morphometric assessment of vertebral deformities is warranted in IBD as well. As a vertebral fracture is a strong predictor of a new fracture of the spine or at other sites, one may wonder whether the high prevalence of vertebral deformities in IBD is a reason for preventive treatment as it is recommended for subjects with increased fracture risk, such as subjects who are treated with supraphysiological doses of glucocorticoids. To support this hypothesis, prospective follow-up data on the development of vertebral deformities in patients with inflammatory bowel disease are needed.

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