ORIGINAL ARTICLE

Prevalence of osteoporosis and osteopenia in patients with inflammatory bowel diseases from Greater Poland Province

Iwona Krela-Kaźmierczak[1], Michał Michalak[2], Aleksandra Szymczak-Tomczak[1], Liliana Łykowska-Szuber[1], Kamila Stawczyk-Eder[1], Katarzyna Waszak[1], Marcin A. Kucharski[1], Agnieszka Dobrowolska[1], Piotr Eder[1]

1 Department of Gastroenterology, Dietetics and Internal Medicine, Poznan University of Medical Sciences, Poznań, Poland
2 Department of Computer Science and Statistics, Poznan University of Medical Sciences, Poznań, Poland

KEY WORDS

inflammatory bowel disease, osteoporosis, osteopenia

ABSTRACT

INTRODUCTION The incidence of osteoporosis in patients with inflammatory bowel disease (IBD) varies across different populations.

OBJECTIVES The aim of this study was to evaluate the prevalence of osteoporosis in Polish patients with IBD, as well as the effect of the body mass index (BMI), disease duration, the number of hospital stays, and the use of glucocorticoids on bone mineral density (BMD).

PATIENTS AND METHODS BMD of 208 patients with IBD (103 with Crohn disease [CD] and 105 with ulcerative colitis [UC]) and 41 healthy controls was measured using dual-energy X-ray absorptiometry. The association of BMD with the other parameters was analyzed using statistical methods.

RESULTS Osteoporosis of the lumbar (L_2–L_4) spine (T-score) was observed in 11.7% of patients with CD and in 3.8% of those with UC, whereas that of the femoral neck (FN), in 5.8% and 2.9% of the patients with CD and UC, respectively. Osteopenia occurred in 35.9% (FN) and 36.9% (L_2–L_4) of CD patients, and in 25.7% (FN) and 29.5% (L_2–L_4) of UC patients. In CD patients, BMI was associated with lumbar and femoral BMD and with L_2–L_4 T-score, whereas FN T-score correlated with BMI. In UC patients, the cumulative glucocorticoid dose correlated with L_2–L_4 T-score, FN BMD, FN T-score, and FN Z-score; the disease duration correlated with FN BMD, while the FN T-score, with the number of hospital stays and FN BMD.

CONCLUSIONS Osteoporosis and osteopenia are frequent in Polish patients with IBD. BMD correlated with BMI in all patients. In UC patients, BMD was associated with the cumulative glucocorticoid dose, disease duration, and number of hospital stays.

Correspondence to:
Iwona Krela-Kaźmierczak, MD, Department of Gastroenterology, Dietetics and Internal Medicine, Poznan University of Medical Sciences, ul. Przybyszewskiego 49, 60-355 Poznań, Poland, phone: +48 61 869 13 43, email: krela@op.pl
Received: March 5, 2018.
Revision accepted: June 8, 2018.
Published online: July 11, 2018.
Conflict of interest: see at the end of text.
Pol Arch Intern Med. 2018; 128 (7-8): 447-454
doi:10.20452/pamw.4292

INTRODUCTION Low bone mineral density (BMD) is an established complication in patients with inflammatory bowel disease (IBD), both Crohn disease (CD) and ulcerative colitis (UC).[1] However, data on the prevalence of skeletal system disorders in different populations of IBD patients show much variability due to different methodologies and sample sizes as well as different geographic locations.[1] In literature, the prevalence of osteoporosis and osteopenia in IBD patients ranges from 2% to 56%.[1-4] The mechanism of osteoporosis development in patients with IBD seems to be multifactorial.[5,6] The subtly higher prevalence of osteoporosis in CD patients has been associated with the localization of the disease in the small intestine and with the intestinal resection causing vitamin D absorption disturbances, malnutrition, and estrogen deficiency.[7] Some studies have shown that IBD patients have a genetic predisposition to develop osteoporosis.[8,9] However, other studies did not confirm this predisposition.[10]

According to Frei et al,[11] the risk factors for osteoporosis in patients with CD include high daily doses of glucocorticoids and long therapy duration, young age at diagnosis (usually meaning

TABLE 1 Risk factors for osteoporosis in inflammatory bowel disease[8-16]

Increasing age
Use of corticosteroids and long therapy duration
Malnutrition
Low BMI, low body mass
Malabsorption of vitamin D, calcium, and vitamin K
Immobilization, number of exacerbations, number of hospital stays
Previous fragility fracture
Hypogonadism, estrogen deficiency
Smoking
Chronic inflammatory state including imbalance of the RANK/RANKL/OPG system
Genetic predisposition to develop osteoporosis

Abbreviations: BMI, body mass index; OPG, osteoprotegerin; RANK, receptor activator of NF-κB; RANKL, receptor activator of NF-κB ligand

a more aggressive disease), history of intestinal resections, use of azathioprine, low body mass, and low body mass index (BMI). Vitamin D and calcium deficiency can also play an important role.[12,13] The etiology of osteoporosis in IBD is multifactorial. Risk factors for osteoporosis in IBD are shown in TABLE 1.[8-16] Dual energy X-ray absorptiometry (DXA) is the gold standard for the measurement of BMD. BMD values are expressed in relation to the mean BMD for young adults (T-score) or to BMD values for individuals matched by age (Z-score). The World Health Organization defines osteopenia as BMD greater than 1 standard deviation (SD) below the mean BMD value for young adults but lower than 2.5 SDs below that value (–1< T-score <–2.5), and osteoporosis, as BMD equal to 2.5 SDs below the mean BMD for young adults or lower (T-score <–2.5).[17]

There is no consensus on screening for osteoporosis in IBD patients, with a plethora of guidelines issued by various organizations. In 2007 guidelines, the British Society of Gastroenterology recommended DXA scans in patients with IBD in case of an ongoing glucocorticoid therapy with doses of 7.5 mg/d or higher for 6 months or longer, or for over 3 months if at least 2 additional risk factors were present out of the following: persistent active IBD, weight loss >10%, BMI <20 kg/m^2, or age over 70 years. DXA scan is also recommended for IBD patients under the age of 65 years, in whom glucocorticoid therapy is planned even if there are no other known risk factors for osteoporosis.[18-20] Other osteoporosis risk factors which are indications for bone densitometry in IBD patients include age above 70 years, persistent disease with an increased activity, disease with poor response to treatment, poor nutritional state, lack of physical activity, use of anticonvulsant medications, osteoporotic fractures, female sex, early menopause (<45 years old), late menarche (>15 years old), short period of fertility (<30 years), familial history of osteoporotic fractures, low calcium intake, poor visual acuity, neuromuscular disturbances, and high alcohol consumption. The guidelines of the American College of Gastroenterology (ACG; 2009 for CD[21] and 2010 for UC)[22] and of the American Gastroenterological Association (AGA; 2003)[23] for DXA in IBD patients are similar. DXA is recommended for patients treated with glucocorticoids for over 3 months or for shorter cyclic periods as well as for patients with persistent active disease. Furthermore, the AGA recommends bone densitometry for IBD patients with a history of bone fractures following a relatively minor trauma, for postmenopausal women, men over 50 years old, and for individuals with hypogonadism.[23] According to the ACG recommendation for osteoporosis screening in IBD patients, also smoking, low BMI, sedentary lifestyle, hypogonadism, increased familial risk, nutritional deficiencies, and age above 60 years are indications for a densitometric analysis.[21,22] According to the European Crohn's and Colitis Organisation guidelines (2010 for CD,[24] and 2013 for UC),[25] frequent use of steroids, persistent disease, and long disease duration are indications for densitometry screening in IBD patients. A control DXA is recommended after 2 to 3 years in patients with normal BMD at the first analysis, and after 1 year in patients treated with glucocorticoids. The major indication for DXA in IBD patients is a long-term steroid therapy (92% of cases), followed by postmenopausal status and history of a low-energy fracture (both about 7% of cases).[24,25] The fact that several organizations associate glucocorticoid use with an increased risk of osteoporosis is noteworthy. Although glucocorticoids are an important group of medications, their prolonged use is associated with side effects, including those involving bone tissue. Glucocorticoids have been shown to impair osteoblast function, induce osteocyte and osteoblast apoptosis, reduce intestinal calcium absorption, increase renal excretion of calcium, and lead to early increase in fracture risk prior to loss of BMD.[14,15,26-28] In direct steroid effects on osteoclasts, the role of the RANK/RANKL/OPG system is emphasized.[29] Except for the negative effects on bone tissue (osteopenia, osteoporosis, aseptic bone necrosis, and myopathies), glucocorticoids have also shown numerous other side effects, including esophagitis, gastritis, peptic ulcer disease, digestive hemorrhage, arterial hypertension, neuropsychiatric and psychiatric disorders, glaucoma, cataract, and metabolic diseases.[14,15]

The knowledge about the need for osteoporosis prophylaxis during glucocorticoid use is insufficient.[28-30] Therefore, the aim of this study was to assess the BMD and the prevalence of osteopenia and osteoporosis in patients with IBD, as well as to evaluate the correlation of BMD with BMI, disease duration, number of hospital stays, and glucocorticoid treatment.

PATIENTS AND METHODS The study included 208 adults diagnosed with IBD (103 patients with CD and 105 patients with UC) at the Department of Gastroenterology, Dietetics and Internal Medicine, Poznan University of Medical

Sciences, and 41 adult healthy controls (volunteers) from Greater Poland Province, an administrative region in Poland. All patients gave their written consent to participate in the study, and the study was approved by the local ethics committee. IBD was diagnosed on the basis of standard endoscopic, histopathologic, and radiologic criteria. The exclusion criteria were as follows: age below 18 years old, pregnancy, presence of other diseases that may affect the BMD (diabetes, liver diseases, chronic kidney diseases, thyroid diseases, rheumatoid arthritis, chronic obstructive pulmonary disease, celiac disease, active neoplastic diseases, other serious diseases, immune diseases, and chronic inflammatory processes), and lack of written consent to participate in the study. All patients included in the study were treated according to the current standards of the Polish Gastroenterology Society and European Crohn's and Colitis Organisation, depending on the clinical situation.

Densitometric measurements of the lumbar spine (L_2–L_4) and femoral neck (FN) of the patients were carried out using DXA with the Lunar DPX-Plus instrument (Lunar Corporation, Madison, Wisconsin, United States). The following densitometric parameters were recorded: BMD, T-score, and Z-score. The T-score was calculated as the difference between the obtained BMD measurement and mean BMD for young adults, divided by SD for young adults. The Z-score was calculated as the difference between the measured BMD value and the mean BMD matched by age divided by SD in the general population.

All patients answered a detailed questionnaire concerning the course of the disease, including questions about the disease duration, the number of hospital stays, and treatment with glucocorticoids during the entire disease course. Glucocorticoid doses were expressed as prednisolone equivalents and converted into a cumulative lifetime dose (mg).

Statistical analysis Data were analyzed using the *t* test. The Mann–Whitney test was used if the variables did not follow the normal distribution, and the Kruskal–Wallis and Dunn's post hoc tests were used for simultaneous comparisons of the study groups (controls, CD patients, and UC patients). Associations between the analyzed variables were evaluated using the Spearman rank correlation coefficient, and their significance was assessed using the *t* test. Nominal data were analyzed by the χ^2 test of independence. The analyses were conducted using statistical software package Statistica PL12 (StatSoft, Inc., Tulsa, Oklahoma, United States). All tests were 2-tailed and considered significant at a *P* value of less than 0.05.

RESULTS Clinical characteristics and bone-related parameters of all study participants are summarized in TABLE 2. The mean (SD) age of all patients with IBD was 37.7 (14.0) years. In the CD group, there were 51 women and 52 men (mean [SD] age, 40.0 [14.1] years and 31.7 [9.9] years, respectively). In the UC group, there were 55 women and 50 men (mean [SD] age, 39.2 [15.4] years and 39.9 [14.6] years, respectively). The control group included 20 women and 21 men (mean [SD] age, 33.8 [10.8] years and 27.1 [3.7] years, respectively). There were significant differences in age between group. Patients with UC were significantly older than controls (TABLE 2).

In the CD group, osteoporosis of the lumbar spine (evaluated based on the L_2–L_4 T-score) occurred in 12 patients (11.7%), osteopenia in 38 patients (36.9%), and normal bone mass in 70 patients (66.7%). For the FN, osteoporosis was observed in 6 patients (5.8%), osteopenia in 37 (35.9%), and normal bone mass in 60 (58.3%). Among UC patients, 4 (3.8%) had osteoporosis in the lumbar spine and 3 (2.9%) in the FN, while 31 (29.5%) had osteopenia in the lumbar spine and 27 (25.7%) in the FN. Normal bone mass in the lumbar spine was found in 70 patients (66.7%) and in the FN, in 75 patients (71.4%). The control group had normal bone mass.

Correlations between the analyzed parameters in study groups are presented in TABLE 2. L_2–L_4 BMD and L_2–L_4 T-score in patients with IBD was different from that of controls ($P < 0.01$). Controls had higher BMD than patients with CD ($P < 0.01$) and those with UC ($P = 0.03$). There were significant differences in the L_2–L_4 Z-score between patients with IBD and controls and between patients with CD alone and controls. Significant differences were also found in BMD and T-scores of the FN between all patients with IBD and controls, with both patients with CD and UC showing significantly lower FN BMD than controls. The FN T-scores were also significantly lower in patients with CD and UC patients than in. The groups differed significantly in FN Z-scores, with significant differences also between patients with CD alone and controls. The groups also differed significantly in BMI. Controls had a significantly higher BMI than patients with CD, and there were significant differences between patients with CD and UC. The number of exacerbations and hospital stays was also significantly different between patients with CD and UC.

The prevalence of osteoporosis, osteopenia, and normal BMD (lumbar spine and FN) in patients with UC and CD in comparison with controls is shown in TABLE 3, while TABLE 4 presents data on the prevalence according to sex. Correlations of L_2–L_4 and FN BMD with age and BMI are shown in TABLES 5 and 6. In CD patients, we found a significant correlation between BMD in the lumbar spine and BMI as well as between the L_2–L_4 T-score and BMI. A significant correlation was also shown between FN BMD and age and BMI as well as between FN T-score and age and BMI. FN Z-score values correlated with BMI. In UC patients, a significant correlation was shown between FN BMD and age, as well as between the FN T-score and age. Finally, in controls,

TABLE 2 Clinical characteristics and bone-related parameters of patients with Crohn disease, ulcerative colitis, and controls

Variable	CD (n = 103)	UC (n = 105)	Controls (n = 41)	*P* value
Sex, female, n (% ±1.96 SE)	51 (49.5 ±9.7)	56 (53.3 ±9.5)	20 (48.8 ±15.3)	0.40[a]
Sex, male, n (% ±1.96 SE)	52 (50.5 ±9.7)	49 (46.7 ±9.5)	21 (51.2 ±15.3)	
Glucocorticoid treatment, n (% ±1.96 SE)	85 (82.5 ±7.3)	71 (67.6 ±9.0)	–	0.01[a]
No glucocorticoid treatment, n (% ±1.96 SE)	18 (17.5 ±7.3)	34 (32.4 ±9.0)	–	
L_2–L_4 BMD, g/cm², mean (SD)	1.1 (0.2)	1.2 (0.1)	1.2 (0.1)	<0.01[b]
				0.08[c]
				<0.01[d]
				0.03[e]
L_2–L_4 T-score, mean (SD)	–0.9 (1.5)	–0.4 (1.2)	0.1 (0.7)	<0.01[b]
				0.04[c]
				<0.01[d]
				0.03[e]
L_2–L_4 Z-score, mean (SD)	–0.5 (1.3)	–0.1 (1.2)	0.1 (0.6)	0.01[b]
				0.65[c]
				0.02[d]
				0.11[e]
FN BMD, g/cm², mean (SD)	0.9 (0.2)	1.0 (0.2)	1.18 (0.2)	<0.01[b]
				0.25[c]
				<0.01[d]
				<0.01[e]
FN T-score, mean (SD)	–0.7 (1.3)	–0.3 (1.2)	0.4 (1.0)	<0.01[b]
				0.21[c]
				<0.01[d]
				<0.01[e]
FN Z-score, mean (SD)	–0.3 (1.1)	0.1 (1.1)	0.4 (1.0)	<0.01[b]
				<0.01[c]
				<0.01[d]
				0.43[e]
Age, y, mean (SD)	35.8 (12.8)	39.6 (15.0)	30.4 (8.6)	<0.01[b]
				0.26[c]
				0.08[d]
				<0.01[e]
BMI, kg/m², mean (SD)	21.5 (3.7)	23.3 (4.3)	24.8 (3.5)	<0.01[b]
				<0.01[c]
				<0.01[d]
				0.08[e]
Cumulative prednisolone dose, mg, mean (SD)	3706.9 (5972.8)	2777.5 (4271.5)	–	0.08[f]
Number of exacerbations, mean (SD)	6.4 (5.6)	5.4 (6.0)	–	0.02[f]
Number of hospital stays, mean (SD)	6.8 (5.9)	3.3 (2.6)	–	<0.01[f]
Disease duration, y, mean (SD)	6.6 (5.1)	7.48 (7.0)	–	0.79[f]

a χ^2 test; **b** CD vs UC vs controls (Kruskal–Wallis test); **c** CD vs UC (post hoc test); **d** CD vs controls (post hoc test); **e** UC vs controls (post hoc test); **f** CD vs UC (Mann–Whitney test)

Abbreviations: BMD, bone mineral density; CD, Crohn disease; FN, femoral neck; L_2–L_4, lumbar spine; UC, ulcerative colitis; others, see **TABLE 1**

L_2–L_4 BMD was significantly correlated with BMI, while L_2–L_4 T-score values correlated with BMI.

Correlations between lumbar and femoral BMD and disease duration, the number of hospital stays, and cumulative prednisolone dose in patients with IBD are summarized in **TABLE 6**. In brief, CD patients were more often treated with glucocorticoids during the entire disease course than UC patients (85 [82.5%] and 71 [67.6%], respectively; $P = 0.01$).

In UC patients, cumulative prednisolone dose significantly correlated with the L_2–L_4 T-score and

TABLE 3 Prevalence of osteoporosis, osteopenia, and normal mineral bone density of the lumbar spine and of the femoral neck, based on T-scores, in patients with Crohn disease, ulcerative colitis, and controls

Study group	Osteoporosis	Osteopenia	Normal bone mass
L_2–L_4			
CD	12 (11.7 ±6.2)	38 (36.9 ±9.3)	53 (51.5 ±9.7)
UC	4 (3.8 ±3.7)	31 (29.5 ±8.7)	70 (66.7 ±9.0)
Controls	0 (0 ±0)	0 (0 ±0)	41 (100 ±0)
FN			
CD	6 (5.8 ±4.5)	37 (35.9 ±9.3)	60 (58.3 ±9.5)
UC	3 (2.9 ±3.2)	27 (25.7 ±8.4)	75 (71.4 ±8.6)
Controls	0 (0 ±0)	0 (0 ±0)	41 (100 ±0)

Data are presented as n (% ±1.96 SE)

Abbreviations: see TABLE 2

TABLE 4 Prevalence of osteoporosis, osteopenia, and normal mineral bone density of the lumbar spine (L_2–L_4 level) and femoral neck based on T-scores in patients with inflammatory bowel disease and controls according to sex

	Total number (n)	Osteoporosis	Osteopenia	Osteoporosis and osteopenia	Normal bone mass
Women					
L_2–L_4					
IBD	106	12 (11.3 ±6.0)	34 (32.1 ±8.9)	46 (43.4 ±9.4)	60 (56.6 ±9.4)
Controls	20	0 (0 ±0)	0 (0 ±0)	0 (0 ±0)	20 (100 ±0)
FN T-score					
IBD	106	7 (6.6 ±4.7)	41 (38.7 ±9.3)	48 (45.3 ±9.5)	58 (54.7 ±9.5)
Controls	20	0 (0 ±0)	0 (0 ±0)	0 (0 ±0)	20 (100 ±0)
Men					
L_2–L_4					
IBD	102	4 (3.9 ±3.8)	35 (34.3 ±9.2)	39 (38.2 ±9.4)	63 (61.8 ±9.4)
Controls	21	0 (0 ±0)	0 (0 ±0)	0 (0 ±0)	21 (100 ±0)
FN T-score					
IBD	102	2 (2 ±2.7)	23 (22.5 ±8.1)	25 (24.5 ±8.3)	77 (75.5 ±8.3)
Controls	21	0 (0 ±0)	0 (0 ±0)	0 (0 ±0)	21 (100 ±0)

Data are presented as n (% ±1.96 SE).

Abbreviations: IBD, inflammatory bowel disease; others, see TABLE 2

50 with UC), osteopenia was found in 50% of patients and osteoporosis, in 15%. Furthermore, patients treated with high doses of steroids were shown to have a higher risk of low BMD.[31] In a study of 37 Italian IBD patients, osteopenia was shown in 43% of patients and osteoporosis, in 11%. The authors suggested performing densitometry in all women newly diagnosed with IBD and in all men above the age of 30 years.[32] A high prevalence of osteoporosis and osteopenia was reported in a Tunisian population of IBD patients. Osteoporosis in the FN was found in 31.8% of CD patients and 13% of UC patients, while that in the lumbar spine, in 40.9% and 8.7% of the patients, respectively. In CD patients, osteoporosis in the FN was more common.[33] A high prevalence of osteoporosis (24.1%) and osteopenia (50.3%) was also found in a study of 200 IBD patients from Iran.[34]

A study of 95 Saudi patients with IBD (46% with CD and 54% with UC) showed a high risk of low BMD, which was associated with BMI and age, but not with steroid use and IBD type. The mean age of patients was similar to that of our subjects (30.9 years [SD, 11.6]). Osteopenia occurred in 44.2% of patients and osteoporosis, in 30.5%, as diagnosed on the basis of the lower lumbar and femoral T-score values. The authors showed that BMI was positively correlated with the Z-score of both the lumbar spine and the FN.[35] In our study, we showed a similar correlation, which allows to identify BMI as an independent risk factor for osteoporosis. A study of 1703 American patients with IBD showed that BMI was the strongest

Z-score. The disease duration and the number of hospital stays significantly correlated with femoral BMD and T-score.

DISCUSSION Osteoporosis and osteopenia often coexist in patients with IBD. In our study, BMD deficiency (osteopenia, osteoporosis) was more frequent in patients with CD than in those with UC. A high prevalence of osteopenia and osteoporosis in the lumbar spine and FN (as evaluated by the T-scores) was shown both in women (43.4% and 45.3%, respectively) and in men (38.2% and 24.5%, respectively).

The results of other studies show considerable discrepancies depending on the population studied, sample size, and the age of patients. In a French study of 84 IBD patients (34 with CD,

TABLE 5 Correlations between bone mineral density and age and morphological features in patients with inflammatory bowel disease compared with controls

Parameter	CD	UC	Controls
L_2–L_4 BMD, g/cm^2			
Age, y	$r = –0.06$; $P = 0.54$	$r = –0.11$; $P = 0.34$	$r = 0.34$; $P = 0.12$
BMI, kg/m^2	$r = 0.34$; $P < 0.01$	r = 0.11; $P = 0.21$	$r = 0.42$; $P < 0.01$
L_2–L_4 T-score			
Age, y	$r = –0.02$; $P = 0.93$	$r = –0.14$; $P = 0.26$	$r = 0.22$; $P = 0.19$
BMI, kg/m^2	$r = 0.32$; $P < 0.01$	$r = 0.1$; $P = 0.24$	$r = 0.31$; $P = 0.04$
L_2–L_4 Z-score			
Age, y	$r = 0.11$; $P = 0.23$	$r = 0.05$; $P = 0.61$	$r = 0.33$; $P = 0.07$
BMI, kg/m^2	$r = 0.12$; $P = 0.13$	$r = –0.04$; $P = 0.64$	$r = 0.02$; $P = 0.93$
FN BMD, g/cm^2			
Age, y	$r = –0.23$; $P = 0.02$	$r = –0.34$; $P < 0.01$	$r = –0.08$; $P = 0.61$
BMI, kg/m^2	$r = 0.33$; $P<0.01$	$r = 0.21$; $P = 0.07$	$r = 0.24$; $P = 0.14$
FN T-score			
Age, y	$r = –0.21$; $P = 0.03$	$r = –0.40$; $P<0.01$	$r = 0.01$; $P = 0.94$
BMI, kg/m^2	$r = 0.34$; $P < 0.01$	$r = 0.10$; $P = 0.37$	$r = 0.14$; $P = 0.41$
FN Z-score			
Age, y	$r = –0.01$; $P = 0.94$	$r = –0.09$; $P = 0.31$	$r = 0.16$; $P = 0.34$
BMI, kg/m^2	$r = 0.21$; $P = 0.03$	$r = 0.08$; $P = 0.48$	$r = –0.02$; $P = 0.93$

Abbreviations: see **TABLES 1** and **2**

TABLE 6 Correlations between bone mineral density and disease duration, number of hospital stays, and cumulative prednisolone dose in patients with Crohn disease and ulcerative colitis

Parameter	CD	UC
L_2–L_4 BMD, g/cm^2		
Cumulative prednisolone dose, mg	$r = –0.09$; $P = 0.44$	$r = –0.11$; $P = 0.27$
Disease duration, y	$r = 0.02$; $P = 0.93$	$r = –0.21$; $P = 0.11$
Number of hospital stays	$r = 0.02$; $P = 0.93$	$r = –0.11$; $P = 0.27$
L_2–L_4 T-score		
Cumulative prednisolone dose, mg	$r = –0.05$; $P = 0.69$	$r = –0.24$; $P = 0.03$
Disease duration, y	$r = 0.04$; $P = 0.71$	$r = –0.21$; $P = 0.07$
Number of hospital stays	$r = 0.04$; $P = 0.71$	$r = –0.14$; $P = 0.19$
L_2–L_4 Z-score		
Cumulative prednisolone dose, mg	$r = –0.06$; $P = 0.53$	$r = –0.21$; $P = 0.06$
Disease duration, y	$r = –0.04$; $P = 0.71$	$r = –0.04$; $P = 0.71$
Number of hospital stays	$r = –0.06$; $P = 0.53$	$r = –0.05$; $P = 0.64$
FN BMD, g/cm^2		
Cumulative prednisolone dose, mg	$r = –0.16$; $P = 0.17$	$r = –0.20$; $P = 0.07$
Disease duration, y	$r = 0.01$; $P = 0.95$	$r = –0.23$; $P = 0.04$
Number of hospital stays	$r = –0.05$; $P = 0.69$	$r = –0.24$; $P = 0.03$
FN T-score		
Cumulative prednisolone dose, mg	$r = –0.20$; $P = 0.08$	$r = –0.19$; $P = 0.06$
Disease duration, y	$r = –0.01$; $P = 0.9$	$r = –0.24$; $P = 0.03$
Number of hospital stays	$r = –0.05$; $P = 0.61$	$r = –0.24$; $P = 0.03$
FN Z-score		
Cumulative prednisolone dose, mg	$r = –0.20$; $P = 0.08$	$r = –0.22$; $P = 0.03$
Disease duration, y	$r = –0.03$; $P = 0.87$	$r = –0.11$; $P = 0.27$
Number of hospital stays	$r = –0.06$; $P = 0.53$	$r = –0.14$; $P = 0.19$

Abbreviations: see **TABLES 1** and **2**

independent risk factor for the development of osteoporosis. The role of age and cumulative steroid dose was also emphasized.[36] Our results show a correlation between cumulative prednisolone dose used in the course of the disease and the L_2–L_4 T-score as well as the FN T-score and Z-score in UC patients. Moreover, the duration of the disease and the number of hospital stays correlated with BMD in these patients. Such an association was not found for CD patients. Similar associations were reported in other studies on glucocorticoid treatment in IBD and its effect on BMD. Ardizzone et al,[37] in a study of Italian patients, showed that only 8% of CD patients (4 of 51) and 15% of UC patients (6 of 40) had normal BMD, 55% of CD patients and 67% of UC patients had osteopenia, and osteoporosis was found in 37% of CD and 18% of UC patients. Similar results were reported by Abitbol et al[31] who found a positive correlation between cumulative steroid dose used during the entire disease course and low BMD in patients with UC, whereas in CD patients, they showed a positive correlation between low BMD and disease duration and patient age. In a cohort study on 253 Swiss patients with IBD, the prevalence of osteopenia and osteoporosis was 57% and 20%, respectively, and it was found to be associated with steroid treatment.[18] A slightly different association was reported by Dumitrescu et al[38] in a prospective study including 143 IBD patients from Romania. Osteopenia was found in 48.07% of patients with UC and in 56.41% of those with CD, while osteoporosis, in 18.26% of patients with UC and 15.3% of those with CD. The authors demonstrated an association between the prevalence of osteopenia and osteoporosis and the use of high glucocorticoid dose in CD patients. They also found that the prevalence of these 2 bone conditions was associated with a BMI of less than 18.5 kg/m^2 in UC patients.[38]

In a population-based study from Sri Lanka, osteoporosis was significantly more common among patients with IBD than in controls (13.5% and 4.5%, respectively). Osteoporosis was more prevalent in patients with UC (14.45%) than in those with CD (10.7%). Only menopause and the use of glucocorticoids were independent risk factors for osteoporosis in patients with IBD. Such an association was not shown for the severity of the disease, number of exacerbations, disease duration, or treatments other than steroids.[39]

In a Polish study including 129 consecutive adult patients with IBD (69 with CD and 60 with UC), Krakowska-Stasiak et al[40] showed a lower frequency of treatment with glucocorticoids than in our study: glucocorticoids were used in 17 patients with UC (28%) and 23 patients with CD (33%).

In summary, we found that osteopenia and osteoporosis are frequent in patients with IBD, both in women and men. BMD correlated with BMI in all patients. In UC patients, BMD also correlated with the use of glucocorticoids (cumulative prednisolone dose), as well as with disease duration and the number of hospital stays.

In conclusion, our study confirms that it is necessary to implement bone densitometry screening in patients with IBD, as well as to undertake preventive and therapeutic measures in patients who already suffering from or are at high risk of osteoporosis. Poor densitometric results will indicate a possible need to reduce glucocorticoid use to prevent further bone density reduction.

ACKNOWLEDGMENTS We would like to honor the memory of Professor Wanda Horst-Sikorska and Professor Krzysztof Linke who passed away while they were still professionally active. For many years, they had been our mentors, supporting us with their knowledge and ideas. This publication is one of the many late fruits of their work and kind guidance. We would also like thank Science to the Point, a biomedical translation and training company, for revising the language and style of the manuscript. The study was financed by the Polish Ministry of Science and Higher Education (no. 402 481 737; to IK-K).

CONTRIBUTION STATEMENT IK-K conceived the concept of the study and coordinated the financial aspects of the project. PE and IK-K contributed to the study design. IK-K, AS-T, LL-S, KW, KS-E, PE, and MAK were involved in data collection. MM, IK-K and AS-T analyzed the data. IK-K, PE, and AD contributed to the interpretation of data and to drafting the article. All authors revised and approved the final version of the manuscript.

CONFLICT OF INTEREST IK-K received travel grants from Alvogen, Abbvie, and Astellas; PE received lecture fees from Abbvie Poland and travel grants from Astellas, Abbvie Poland, and Ferring; AD received travel grants from Alvogen, Abbvie, and Astellas and lecture fees from Abbvie Poland and Alvogen; LL-S received travel grants from Alvogen, Astellas, and Abbvie Poland; AST received a travel grant from Abbvie Poland; MAK and KSE received travel grants from Alvogen. KW and MM have nothing to disclose.

REFERENCES

1 Pigot F, Roux C, Chaussade S, et al. Low bone mineral density in patients with inflammatory bowel disease. Dig Dis Sci. 1992; 37: 1396-1403.

2 Mueller D, Gandjour A. Cost-effectiveness of using clinical risk factors with and without DXA for osteoporosis screening in postmenopausal women. Value Health. 2009; 8: 1106-1117.

3 Arden NK, Cooper C. Osteoporosis in patients with inflammatory bowel disease. Gut. 2002; 50: 9-10.

4 Sapone N, Pellicano R, Simondi D, et al. A 2008 panorama on osteoporosis and inflammatory bowel disease. Minerva Med. 2008; 99: 65-71.

5 Loftus EV Jr, Achenbacha SJ, Sandborn WJ, et al. Risk of fracture in ulcerative colitis: a population-based study from Olmsted County, Minnesota. Clin Gastroenterol Hepatol. 2003; 1: 465-473.

6 Krela-Kaźmierczak I, Szymczak A, Łykowska-Szuber L, et al. Osteoporosis in gastrointestinal diseases. Adv Clin Exp Med. 2016; 1: 185-190.

7 Bernstein CN, Leslie WD. The pathophysiology of bone disease in gastrointestinal disease. Eur J Gastroenterol Hepatol. 2003; 15: 857-864.

8 Bartram SA, Peaston RT, Rawlings DJ, et al. Mutifactorial analysis of risk factors for reduced bone mineral density in patients with Crohn's disease. World J Gastroenterol. 2006; 12: 5680-5686.

9 Krela-Kaźmierczak I, Kaczmarek-Ryś M, Szymczak A, et al. Bone metabolism and the c.-223C > T polymorphism in the 5'UTR region of the osteoprotegerin gene in patients with inflammatory bowel disease. Calcif Tissue Int. 2016; 6: 616-624.

10 Krela-Kaźmierczak I, Michalak M, Wawrzyniak A, et al. The c.29T>C polymorphism of the transforming growth factor beta-1 (TGFB1) gene, bone mineral density and the occurrence of low-energy fractures in patients with inflammatory bowel disease. Mol Biol Rep. 2017; 6: 455-461.

11 Frei P, Fried M, Hungerbuhler V, et al. Analysis of risk factors for low bone mineral density in inflammatory bowel disease. Digestion. 2006; 1: 40-46.

12 Krela-Kaźmierczak I, Szymczak A, Tomczak M, et al. Calcium and phosphate metabolism in patients with inflammatory bowel diseases. Pol Arch Med Wewn. 2015; 7-8: 588-590.

13 Bours PH., Wielders JP, Vermeijden JR, et al. Seasonal variation of serum 25-hydroxyvitamin D levels in adult patients with inflammatory bowel disease. Osteoporos Int. 2011; 11: 2857-2867.

14 Bernstein CN, Leslie WD. The pathophysiology of bone disease in gastrointestinal disease. Eur J Gastroenterol Hepatol. 2003; 8: 857-864.

15 Recommendations for the prevention and treatment of glucocorticoid--induced osteoporosis. American College of Rheumatology Task Force on Osteoporosis Guidelines. Arthritis Rheum. 1996; 11: 1791-1801.

16 Ali T, Lam D, Bronze MS, Humphrey MB. Osteoporosis in inflammatory bowel disease. Am J Med. 2009; 7: 599-604.

17 Gluszko P, Lorenc RS, Karczmarewicz E, et al. Working Group including the representatives of the Polish Associations of Orthopedics and Traumatology, Rehabilitation, Gerontology, Rheumatology, Family Medicine, Diabetology, Laboratory Diagnostics, Andropause and Menopause, Endocrinology, Radiology, and the STENKO group. Polish guidelines for the diagnosis and management of osteoporosis: a review of 2013 update. Pol Arch Med Wewn. 2014; 5: 255-263.

18 Schüle S, Rossel JB, Frey D, et al. Widely differing screening and treatment practice for osteoporosis in patients with inflammatory bowel diseases in the Swiss IBD cohort study. Medicine (Baltimore). 2017; 96: 22.

19 Guidelines for osteoporosis in inflammatory bowel disease and coeliac disease. Written and approved by the British Society of Gastroenterology June 2007. https://www.bsg.org.uk/resource/guidelines-for-osteoporosis-in-inflammatory-bowel-disease-and-coeliac-disease.html. Published June 1, 2007. Accessed August 24, 2018.

20 Scott EM, Gaywood I, Scott BB. Guidelines for osteoporosis in coeliac disease and inflammatory bowel disease. Gut. 2000; 46, 1: 1-8.

21 Lichtenstein GR, Hanauer SB, Sandborn WJ. Practice Parameters Committee of the American College of Gastroenterology. Management of Crohn's disease in adults. Am J Gastroenterol 2009; 104: 465-483.

22 Kornbluth A, Sachar DB. MACG and The Practice Parameters Committee of the American College of Gastroenterology. Ulcerative Colitis Practice Guidelines in Adults: American College of Gastroenterology, Practice Parameters Committee Am J Gastroenterol. 2010; 105: 501-523.

23 Bernstein CN, Leslie WD, Leboff MS. AGA technical review on osteoporosis in gastrointestinal diseases. Gastroenterology 2003; 3: 795-841.

24 Van Assche G, Dignass A, Panes J, et al. European Crohn's and Colitis Organisation (ECCO). J Crohns Colitis. 2010; 1: 7-27.

25 Van Assche G, Dignass A, Bokemeyer B, et al. European Crohn's and Colitis Organisation. Second European evidence-based consensus on the diagnosis and management of ulcerative colitis part 3: special situations. J Crohns Colitis. 2013; 1: 1-33.

26 Whittier X, Saag KG. Glucocorticoid-induced osteoporosis. Rheum Dis Clin North Am. 2016; 1: 177-189.

27 Longui CA. Glucocorticoid therapy minimizing side effects. J Pediatr (Rio J). 2007; 5: 163-177.

28 Pereira RM, Carvalho JF, Paula AP, et al. Committee for Osteoporosis and Bone Metabolic Disorders of the Brazilian Society of Rheumatology; Brazilian Medical Association; Brazilian Association of Physical Medicine and Rehabilitation. Guidelines for the prevention and treatment of glucocorticoid--induced osteoporosis. Rev Bras Reumatol. 2012; 4: 580-593.

29 Sewerynek E. [Current indications for prevention and therapy of steroid-induced osteoporosis in men and women]. Endokrynol Pol. 2011; 62 Suppl 2: 1-8. Polish.

30 Papierska L, Rabijewski M. Glucocorticoid-induced osteoporosis. Pol Arch Med Wewn. 2007; 8: 363-369.

31 Abitbol V, Roux C, Chaussade S, et al. Metabolic bone assessment in patients with inflammatory bowel disease. Gastroenterology. 1995; 108: 417-422.

32 Adriani A, Pantaleoni S, Luchino M, et al. Osteopenia and osteoporosis in patients with new diagnosis of inflammatory bowel disease. Panminerva Med. 2014; 2: 145-149.

33 Boubaker J, Feki M, Hsairi M, et al. Osteoporosis and inflammatory bowel disease: prevalence and risk factors in Tunisian patients. Gastroenterol Clin Biol. 2003; 10: 901-907.

34 Shirazi KM, Somi MH, Rezaeifar P, et al. Bone density and bone metabolism in patients with inflammatory bowel disease. Saudi J Gastroenterol. 2012: 4: 241-247.

35 Ismail MH, Al-Elq AH, Al-Jarodi ME, et al. Frequency of low bone mineral density in Saudi patients with inflammatory bowel disease. Saudi J Gastroenterol. 2012; 18: 201-207.

36 Atreja A, Aggarwal A, Licata AA, et al. Low body mass index can identify majority of osteoporotic inflammatory bowel disease patients missed by current guidelines. ScientificWorldJournal. 2012; 807 438: 1-6.

37 Ardizzone S, Bollani S, Bettica P, et al. Altered bone metabolism in inflammatory bowel disease: there is a difference between Crohn's disease and ulcerative colitis. J Intern Med. 2000; 247: 63-70.

38 Dumitrescu G, Mihai C, Dranga M, et al. Bone mineral density in patients with inflammatory bowel disease from north-eastern Romania. Rev Med Chir Soc Med Nat Iasi. 2013; 117: 23-28.

39 de Silva AP, Karunanayake AL, Dissanayaka TG, et al. Osteoporosis in adult Sri Lankan inflammatory bowel disease patients. World J Gastroenterol. 2009; 28: 3528-3533.

40 Krakowska-Stasiak M, Cibor D, Domagała-Rodacka R, et al. Insulin-like growth factor system in remission and flare of inflammatory bowel diseases. Pol Arch Intern Med. 2017; 12: 832-839.