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ORIGINAL ARTICLE

Influence of Risk Factors on Bone Density in Inflammatory Bowel Diseases

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Abstract

Background/Aim: Young people and teenagers are often affected by chronic inflammatory bowel diseases, such as ulcerative colitis and Crohn disease. Prolonged and continuous inflammation, the release of inflammatory mediators with increased osteoclastic activity and reduced osteoblast activity, lead to accelerated bone mineral loss. Glucocorticoid (GC) utilisation in the pharmacotherapy of inflammatory bowel disease (IBD) and malabsorption are additional risk factors affecting bone mineral density (BMD). The main objective of this research was to assess the influence smoking, coffee, alcohol, physical activity and therapy on BMD in chronic inflammation the digestive system.

Methods: A retrospective study included 30 respondents with IBD, average age 34.0 ± 6.73. Participants were divided according to the type of disease into the categories of Crohn disease - CD (n = 14) and ulcerative colitis - UC (n = 16). All patients had their BMD determined by osteodensitometry.

Results: Osteopenia was present in 56.7 % of patients. A statistically significantly higher percentage of patients with UC had osteopenia (40 % vs 16.7 %, $p < 0.05$). Osteoporosis (OP) was not recorded in the study participants. Smoking and coffee consumption were the most common risk factors. Studying risk factors showed that treatment with GC therapy led to a statistically markedly reduced BMD in form of osteopenia in respondents with UC (40 % vs CD 16.7 %, $p < 0.05$).

Conclusion: Presented study's findings indicated that 50 % of the patients presented with reduced BMD in the form of osteopenia, which was more present in UC patients. In this study, only the use of GC had a statistically significant negative effect on BMD.

Key words: Colitis, ulcerative; Crohn disease; Inflammatory bowel diseases; Bone diseases, metabolic.

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Introduction

The chronic nature of inflammatory bowel diseases (IBD) most commonly occurs in younger individuals and adolescents and includes Crohn disease (CD) and ulcerative colitis (UC). The diagnosis of the disease is made based on clinical, endoscopic and histopathological criteria.[1] Prolonged inflammation, recurrent diarrhoea and abdominal pain are accompanied by fatigue and gastrointestinal bleeding. In addition to gastrointestinal involvement, 50 % of affected individuals exhibit extraintestinal manifestations of the disease,[2] such as osteopenia and osteoporosis

characterised by bone loss and low bone mineral density (BMD).[3] Aging and the slowing of regenerative processes augment the likelihood of bone mass depletion loss. Chronic inflammation, which reduces BMD, increases the risk of osteoporosis (OP) and subsequent fractures in patients. During periods of disease activity, approximately 50 % of patients may experience complications due to reduced nutrient absorption, thereby increasing the risk of OP.[4] The aetiology of OP is complex and is still being researched, application of glucocorticoid (GC), low body weight, reduced physical activity, smoking, alcohol and coffee consumption are known risk factors. While GC were once thought to be the leading cause of osteoporosis, research showed that even patients without GC exposure can experience reduced BMD. A key factor in this process is the stimulation of osteoclastogenesis by chronic inflammation and the release of interleukins 1, 6, 11, 15 and 17 as well pro-inflammatory cytokine TNF-alpha,[4] which plays an important role in bone loss in CD.[3] Alcohol and smoking as risk factors affect bone health by reducing calcium absorption, interfering with vitamin D synthesis, lowering oestrogen levels, increasing the risk of falls, damaging blood vessels and reducing osteoblast activity. Caffeine found in products like coffee can negatively impact bone structure, as its consumption may decrease bone density, thereby increasing the risk of OP and other bone changes.[5] Bone density reaches its peak between the ages of 25 and 30. A significant proportion of individuals with IBD are younger, making physical activity crucial for bone health.[2, 5]

This study investigated the significance smoking, caffeinated and alcoholic beverages, physical activity and therapy on BMD in IBD patients.

Methods

Retrospective research presented as a pilot study, on a sample of 30 respondents, 18 male and 12 female, over a period of 9 months, who were classified according to IBD type: the CD group (N = 14) and the UC group (N = 16) was performed. Clinical presentation, in conjunction with endoscopic examination and histopathological findings of intestinal biopsy samples confirmed the diagnosis of IBD. Assessment BMD at the femoral neck and lumbar spine was measured using a (DEXA) densitometer *Hologic QDR1000*, manufactured by *GE Medical Systems* in the USA. T-scores (young adult) and Z-scores (age-and race-matched) were used to present DEXA results expressed in g/cm^2. The guidelines issued by the World Health Organization (WHO) indicate recommendations that T-score greater than -1 be classified as normal, -1 and -2.5 as osteopenia and below of -2.5 or less be OP.[7] The Z-score is used for interpreting BMD in men under 50 years, premenopausal women and children. A Z-score below -2 is defined as low BMD.[6] As presented study included premenopausal women and men under 50 years, BMD parameters were estimated and reported using the values of both scores. Data regarding smoking, coffee, alcohol consumption, physical activity and glucocorticoid and azathioprine therapy were collected through patient anamnesis and review of medical records. The level of physical activity was classified into mild, moderate and intense. Mild activity included walking without difficulty breathing, cooking and balance exercises. Moderate activity included gardening, cycling, brisk walking, or light jogging. Intense physical activity encompassed high-intensity exercises such as weight training, sprinting, rowing machine workouts, swimming, or competitive rowing.

Statistical analysis

Descriptive statistical methods were used for data analysis. The results were presented in tabular form. Statistical analysis was performed in SPSS Programme v 20.0, values of $p < 0.05$ were considered statistically significant. Results were presented as mean ± standard deviation (SD). Statistical comparisons were performed using Student's t-test and Chi-square test for continuous and categorical variables.

Results

Table 1 summarises the participants' demographic and clinical characteristics. While patients with CD had a higher BMI, this difference was not statistically significant. Normal BMD was observed in 41.9 % of participants, while osteopenia was present in 56.7 %. Significantly more UC patients (40 %) had osteopenia compared to CD patients (16.7 %, $p < 0.05$). Osteoporosis was not detected in any participant. Among risk factors, smoking was reported by 51.6 % of patients, with a higher

Table 1: Parameters of patients with inflammatory bowel disease (IBD)

Parameter	CD	UC	p-value
Gender (M/F)	8/6	10/6	ns
Age, years	34.86 ± 6.56	33.60 ± 6.60	ns
Weight, kg	78.50 ± 13.10	74.20 ± 12.00	ns
Height, cm	174.78 ± 8.57	176.68 ± 9.60	ns
BMI, kg/m^2	25.90 ± 3.90	23.60 ± 3.01	ns
L1-L4, T-score	0.27 ± 1.04	-0.39 ± 1.40	ns
L1-L4, Z score	0.26 ± 0.90	-0.25 ± 1.80	ns
RF, T-score	0.17 ± 0.92	-0.14 ± 1.29	ns
RF, Z score	0.15 ± 0.05	-0.12 ± 0.88	ns
LF, T-score	0.17 ± 0.92	-0.38 ± 1.04	ns
LF, Z score	0.18 ± 0.78	-0.35 ± 0.97	ns

Results are presented as mean ± standard deviations; ns - non-significant (p > 0.05); CD - Crohn disease; UC - Ulcerative colitis; M-male; F- female; BMI-body mass index; L1-L4- lumbar vertebrae from one to four vertebrae; RF -Right femur; LF- Left femur;

prevalence among UC patients (43.3 %) compared to CD patients (10.0 %). Coffee consumption was reported by 74.2 % of participants, while no participant reported alcohol consumption.

All patients in the study engaged in some form of physical activity, whether mild, moderate, or intense. The majority of participants engaged in moderate physical activity (50 %), while 36 % engaged in mild activity. Intensive physical activity was practiced by approximately 13.3 % of patients. The relationship between the therapy used for treating IBD and changes in BMD showed varying results. All patients in the study were receiving biological therapy, while some also used glucocorticoids or the immunosuppressive drug azathioprine. Although around 13 % of patients in both groups used glucocorticoids, osteopenia was noted in 40 % of participants with UC compared to 16.7 % of CD. (Table 2).

Table 2: Osteopenia distribution by inflammatory disease type

Parameter	BMD		p-value
	Normal	Osteopenia	
Crohn diseas	9 (30.0 %)	5 (16.7 %)	ns
Ulcerative colitis	4 (4.0 %)	12 (40.0 %)	p < 0.05

BMD - bone mineral density; ns- not significant (p > 0.05);

Table 3: Distribution in relation to therapy

Parameter	Crohn disease	Ulcerative colitis	Osteopenia	p-value
Glucocorticoids	4 (13.3 %)	4 (13.3 %)	8 (26.6)	p < 0.05*
Azathioprine	2 (6.7 %)	6 (20.0 %)	8 (26.7)	ns

**X^2 = 4.224, df = 1, p = 0.04; ns- not significant;*

A statistically meaningful lower BMD was present in the those with UC. Azathioprine use did not show association between its use and changes in BMD in either patient cohort (Table 3).

Discussions

Inflammatory bowel diseases, according to epidemiological data, occur between the ages of 15 and 40, affecting both genders equally. In presented study, the average age of participants fell within this range, consistent with other studies, without statistically significant differences by gender.[7, 8] Bone loss in IBD has multiple causes. The primary risk factors include therapy, smoking, coffee and alcohol consumption, nutritional status and insufficient physical activity.[2, 5]

Presented study data showed that none of the participants had osteoporosis. Half of the participants had osteopenia, with a significantly higher percentage among those with ulcerative colitis. The same indicators were shown in the Schule study in which osteopenia was recorded in 57 % of participants, compared to 20 % OP.[9] A study Yi et al in China, using a cross-sectional design, confirmed osteopenia in 24.6 % of participants,[10] with similar results found by Ratajczak et al.[11]

The nutritional status of presented participants, determined by BMI, showed normal weight among ulcerative colitis patients, while CD patients were categorised as overweight. Several studies have confirmed the link between lower BMI and bone changes, including Azzopardi's and Atreja's research groups.[12, 13] Contrary to expectations, presented findings did not establish a significant association between BMI and decreased bone mineral density. Smoking as a risk factor did not show an association with bone changes in this study. Research on the link between tobacco use and BMD have confirmed its negative impact in worsening CD, though no significant effect was found for UC.[5, 14, 15] Caffeine may negatively affect bone structure, though the direct correlation remains unclear. Coffee consumption can reduce bone density, thereby increasing the risk of osteoporosis.[5, 15] Although two-thirds of presented participants consumed coffee, no clear relationship was established. Bergmann's study proved the negative impact of alcohol on BMD, though without a specific impact on disease progression.[16] Since participants denied alcohol con-

sumption, we were unable to examine this correlation. Physical activity reduces stress, anxiety and depression, which are very common in these cases. Physical activity reduces stress, anxiety and depression, which are very common in these cases. It also affects intestinal function by accelerating peristalsis, improving digestion and reducing bloating. Moderate exercise, particularly strength training, can help maintain and increase muscle mass.[17, 18] Previous studies that used the International Physical Activity Questionnaire (IPAQ) to assess the physical activity of patients with IBD confirm a level of physical activity of up to 27.2 %.[19] A study by Holik et al confirmed that daily physical activity positively influences disease progression, as patients who did not use therapy for IBD were in remission, suggesting the importance of physical activity in disease management.[17] A similar study in the UK found that 72 % of those who exercised regularly reported improved disease control, sleep quality and weight regulation. Sigurdsson investigated how childhood exercise regimen affected BMD of patients with IBD. These, 57 % reported not engaging in significant physical activity in their youth, defined as exercising more than four hours per week.[18] Resistance and/or strength training appeared to be the most effective, as they improved BMD, particularly in older adults and postmenopausal women.[19] Presented study results showed that most patients engaged in moderate physical activity, which did not significantly impact disease progression or the occurrence of bone changes associated with decreased BMD. Due to the reduction of inflammation, GC are commonly employed in the management of IBD helping to reduce symptoms in the acute phase when inflammation is most severe. Because of corticosteroid treatment, frequent hospitalisations, nutritional deficiencies and systemic inflammation, patients with IBD are vulnerable to BMD loss.[20] Although their beneficial effects in treatment are undeniable, long-term use can reduce bone density, lead to osteoporosis and increase fracture risk.[15, 21] Abraham et al confirmed that the risk is twice as high in patients using glucocorticoids.[22] About 50 % of patients on long-term glucocorticoid therapy will develop osteopenia and fractures, with 17 % experiencing fractures within the first year of treatment.[23] Osteopenia prevalence was significantly higher in UC patients, while immunosuppressive drugs, such as azathioprine, can induce IBD remission, may also contribute to osteopenia.[24] However, no statistical significance was found between azathioprine use and BMD in presented participants.

Conclusion

Presented study demonstrated that half of the patients exhibited reduced BMD in the form of osteopenia, which was significantly more frequent in UC patients. Among the examined risk factors, only glucocorticoid use was associated with osteopenia development. The assessment of other risk factors showed that there was no clear evidence of a strong influence on bone mineral density. This pilot study would serve as a basis for future prospective studies on a larger sample.

Ethics

This research was approved by the Ethics Committee University Clinical Centre of the Republic of Srpska, decision No 01-17-321-2/23, dated 3 December 2023.

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Conflicts of interest

The authors declare that there is no conflict of interest.

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Data access

The data that support the findings of this study are available from the corresponding author upon reasonable individual request.

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