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The Effect of Body Composition on Osteoporosis Risk in Adults with Celiac Disease

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Abstract: Background: Celiac disease (CD) has been linked with increased susceptibility to osteoporosis; therefore, we aimed to explore whether, in a group of patients with CD, body composition parameters impact bone parameters. **Methods:** This study covered 56 adults—47 women and 9 men—with CD, and 20 healthy controls—16 women and 4 men. Densitometry of the lumbar spine (L1–L4) and femoral neck (FN) was conducted using dual-energy X-ray absorptiometry (DXA). Body mass was measured by bioimpedance method. Furthermore, serum 25(OH)D and ionized calcium concentration were determined. **Results:** We found osteopenia in the FN in 19.65% of patients and in L1–L4 in 26.79% of the patients. One patient displayed evidence of osteoporosis in the L1–L4 region, while two patients (3.57%) exhibited similar findings in the FN. Significant positive correlations were observed between bone mineral density (BMD) and body mass, fat-free mass (FFM), muscle mass, and basal metabolic rate (BMR) for both L1–L4 and the FN, and body mass index (BMI) of L1–L4. **Conclusions:** In conclusion, people with CD are at an increased risk of decreased BMD. Patients with lower body mass, FFM, muscle mass, BMI, and BMR more often present with osteopenia and osteoporosis.

Keywords: celiac disease; bioimpedance analysis; osteoporosis; dual-energy X-ray absorptiometry; body composition

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1. Introduction

Celiac disease (CD) is a chronic, small intestinal enteropathy caused by exposure to gluten among genetically predisposed individuals [1]. The worldwide prevalence of CD is estimated to be 0.7–1.4% of the general population [2]. Recently the clinical presentation of CD has changed, with non-classical CD characterized by extraintestinal manifestation being more common than a classical form of the disease with the domination of gastrointestinal symptoms [3].

Decreased bone mineral density (BMD), which can further develop into osteoporosis, is one of the most frequent extraintestinal symptoms [3,4]. Osteoporosis is a skeletal disorder characterized by a significant loss of bone mass, contributing to increased bone fragility and a higher risk of bone fractures [5]. Current data report that 30–60% of newly diagnosed patients with CD show decreased BMD and 18–35% present with osteoporosis [6–9]. The mechanism of osteoporosis in CD is multifactorial and includes such elements as celiac disease-related local and systemic inflammation [10–12] and deficiency of vitamin D together with impaired calcium absorption, leading to secondary

hyperparathyroidism and increased bone resorption [13]. Moreover, since CD is an inflammatory disease proceeding with malabsorption, patients at diagnosis present with lower mean body mass index (BMI) than the general population. Interestingly, it has been observed that the nutritional status of CD patients diagnosed in recent years is better than that of those diagnosed in earlier years. It is also interesting to note that more patients are overweight and obese at the time of diagnosis; in Western countries, it is estimated that between 15 and 31% of people with celiac disease are overweight at the time of diagnosis and between 6.8 and 13% have obesity [14,15].

Therefore, the aim of this study was to examine the relation between body composition and bone mineral density with the prevalence of osteopenia and osteoporosis in patients with celiac disease.

Given the increasing prevalence of CD and the frequent association between bone disease and prolonged or inadequate treatment, it seems worthwhile to explore the possibility of body composition testing with bioelectrical bioimpedance analysis (BIA) as a potential indicator of increased risk of bone disease in the celiac disease population.

2. Materials and Methods

2.1. Study Population

This observational study comprised 76 adults: 56 adults—47 women and 9 men—with CD treated in the outpatient clinic of the Department of Gastroenterology, Dietetics and Internal Medicine of Poznan University of Medical Sciences and a control group of 20 healthy individuals—16 women and 4 men. Before starting examinations, all the patients provided their written informed consent.

The diagnosis of CD was based on clinical, histopathological—an evaluation of the sections from the duodenal bulb and the distal part assessed with the Marsh scale [16]—and serological criteria—determination of total IgA and antibodies to tissue transglutaminase in the IgA class (anti-tTg IgA). The exclusion criteria were as follows: age <18 and >50 years, menopause in women, pregnancy, glucocorticoid use, the coexistence of diseases that additionally affect the nutritional status and BMD, Crohn's disease or ulcerative colitis, active neoplastic disease, decomposed hyperthyroidism, liver failure, chronic kidney disease, rheumatoid arthritis, chronic obstructive pulmonary disease, and a lack of written informed consent to participate in this study. All patients enrolled in this study were treated according to current standards and remained on a gluten-free diet (GFD). In addition, 78.5% of the patients included in this study had been diagnosed with CD for at least one year before qualification for study group and had remained on a GFD. The mean duration of the disease was 10.69 years. The participants in the control group did not present any clinical symptoms before enrollment in this study and exhibited negative tissue transglutaminase antibodies in the IgA class with IgA determination.

2.2. Bone Assessment

Densitometric measurements of the lumbar spine (L1–L4) and the femoral neck (FN) were carried out using dual-energy X-ray absorptiometry (DXA) with Lunar DPX-Plus (Lunar, Inc., Madison, WI, United States) apparatus. BMD, T-score, and Z-score parameters were obtained to assess skeletal status. The T-score represented the difference between the obtained BMD result and the mean BMD for young adults divided by the standard deviation (SD) for young adults. The Z-score was calculated as the difference between the measured BMD and the age-adjusted mean BMD divided by the SD in the general population.

2.3. Anthropometric Parameters

In both groups, we determined the following body composition parameters: body mass in kg, BMI, fat%, fat tissue mass in kg, visceral fat, muscle mass, fat-free mass (FFM), and basal metabolic rate (BMR). Body composition analyses were performed in the morning, after a night-long rest, and when fasting. During measurements, the patients were wearing

light clothes and no shoes. Body mass was measured with the use of the bioimpedance method (TANITA MC-980 MA, Tanita, Tokyo, Japan) to the nearest 0.01 kg.

2.4. Biochemical Testing and Questionnaire

Additionally, serum 25(OH)D and ionized calcium were determined in a hospital laboratory, using, respectively, the electrochemiluminescence binding method test and ion-selective electrodes. All patients and controls completed an original questionnaire on to their supplementation of vitamin D and calcium.

2.5. Statements

The Bioethics Committee of Poznan University of Medical Sciences approved the study protocol (number 824/21 of 4 November 2021). This study was conducted in accordance with the guidelines included in the Declaration of Helsinki.

2.6. Statistical Methods

The continuous variables were reported as medians and interquartile ranges (Q 1–Q 3) since they did not follow the normal distribution (Shapiro–Wilk test). The categorical data were presented as frequencies and percentages. The comparison of interval parameters between the two groups was performed by Student's *t*-test and the Mann–Whitney U test. The categorical data were analyzed by the chi-square test for independence. Spearman's rank correlation coefficient assessed the relationship between two interval variables. A multiple regression analysis was performed to find significant factors influencing the BMD and T-score results. The analysis was performed using the statistical package Statistica, version 13, developed by TIBCO Software Inc., Palo Alto CA, USA, (2017) https://www.tibco.com/, accessed on 28 July 2024. All tests were considered significant at $p < 0.05$.

3. Results

This study involved 56 adults with celiac disease and 20 healthy adults. The mean age of patients with celiac disease in the study group is 39 years, while in the control group, it is 38 years. The male population represented 16% ($n = 9$) of the celiac disease group, while in the control group, men constituted 20% ($n = 4$) of the group.

The characteristics of the study groups are shown in Table 1. The results show that there are no statistically significant differences in age, body mass, BMI, fat content, visceral tissue, muscle mass, and fat-free mass between the two groups. The patients in the study group have statistically significantly lower values in the following parameters: FN BMD, FN T-score, FN Z-score, L1–L4 BMD, L1–L4 T-score.

The patients with celiac disease were more likely to report supplementation of vitamin D and calcium—88% ($n = 44$) and 24.49% ($n = 12$), respectively—than were controls—38.89% ($n = 7$) reported supplementation of vitamin D and none reported supplementation of calcium. Interestingly, the patients with CD have higher vitamin D concentrations compared to the control group—36 ng/dL (30.00–49.00) vs. 30 ng/dL (25.00–32.00)—but lower serum concentrations of ionized calcium—5.25 mg/dL (5.23–5.51) vs. 5.38 mg/dL (5.29–5.49).

Based on the T-score, the patients were divided into groups with normal and decreased BMD—osteopenia or osteoporosis—of the FN and L1–L4. Statistically significant differences were observed in the prevalence of decreased BMD of the FN ($p = 0.032$) and L1–L4 ($p < 0.001$) between both groups. The prevalence of osteopenia and osteoporosis based on the T-score is higher in a group of CD patients. The outcomes are presented in Tables 2 and 3.

Table 1. The characteristics of the study group.

Parameter	CD (n = 56)	CG (n = 20)	p-Value
Age, years	39 (32; 44)	38 (26; 43.5)	0.6
Body mass, kg	61 (56.7; 69.4)	66.9 (57.5; 72.5)	0.16
BMI, kg/m^2	21.5 (20; 23.6)	22.4 (20.9; 24.4)	0.24
Fat tissue, kg	14.15 (11.25; 21.42)	18.74 (15.27; 23.05)	0.24
Visceral tissue	3 (1; 4)	3.5 (2; 4)	0.4
Muscle mass, kg	43.15 (40.3; 48.3)	47.15 (42.3; 50.5)	0.18
Fat-free mass, kg	45.85 (42.4; 50.9)	49.50 (45; 53.2)	0.09
BMD (FN), g/cm^2	0.9915 (0.921; 1.043)	1.077 (0.997; 1.193)	<0.001
T-score (FN)	−0.3 (−0.7; 0.2)	0.3 (−0.15; 1.25)	<0.001
Z-score (FN)	0.1 (−0.4; 0.5)	0.5 (0.05; 1.3)	0.02
BMD (L1–L4), g/cm^2	1.605 (1.066; 1.274)	1.207 (1.17; 1.3)	<0.01
T-score (L1–L4)	−0.300 (−1.2; 0.7)	0.2500 (−0.3; 1.05)	<0.001
Z-score (L1–L4)	0.0 (−0.9; 0.7)	0.45 (−0.15; 1)	0.14
BMR	1365 (1285; 1486)	1493 (1341; 1615)	0.11

Data are shown as median and interquartile ranges. p-values < 0.05 are considered significant. Abbreviations: BMD, bone mineral density; BMI, body mass index; BMR, basal metabolic rate; CD, celiac disease; CG, control group; FN, femoral neck; L1–L4, lumbar spine.

Table 2. Prevalence of decreased BMD (based on the T-score) of the FN in the study group.

Femoral Neck, BMD	CD (n = 56)	CG (n = 20)	p-Value
Normal (T-score > −1.0)	45 (80.36%)	20 (100%)	p = 0.032
Osteopenia	9 (16.07%)	0 (0%)	
Osteoporosis (T-score ≤ −2.5)	2 (3.57%)	0 (0%)	

p-values < 0.05 are considered significant. Abbreviations: BMD, bone mineral density; CD, celiac disease; CG, control group.

Table 3. Prevalence of decreased BMD (based on the T-score) of the L1–L4 in the study group.

L1–L4, BMD	CD (n = 56)	CG (n = 20)	p-Value
Normal (T-score > −1.0)	41 (73.21%)	18 (95%)	<0.001
Osteopenia	14 (25.00%)	1 (5.00%)	
Osteoporosis (T-score ≤ −2.5)	1 (1.79%)	0 (0%)	

p-values < 0.05 are considered significant. Abbreviations: BMD, bone mineral density; CD, celiac disease; CG, control group; L1–L4, lumbar spine.

Further, we performed a linear regression analysis. In the univariate regression model, the CD group showed a significant positive correlation between femoral neck BMD and body mass, fat-free mass, muscle mass, and BMR. The data are presented in Table 4.

In the univariate regression model, the CD group showed a significant positive correlation between L1–L4 BMD and body mass, fat-free mass, muscle mass, BMI, and BMR. The data are presented in Table 5.

Table 4. The results of the univariate linear regression model in the study and control group for femoral neck BMD.

Variable	Group	R	T	*p*-Value
Body mass, kg	CD	0.407	3.023	0.004
	CG	0.491	2.396	0.028
Fat tissue, kg	CD	0.099	0.667	0.508
	CG	0.363	1.655	0.115
Fat-free mass, kg	CD	0.42	3.192	0.003
	CG	0.28	1.241	0.23
Muscle mass, kg	CD	0.4	2.947	0.005
	CG	0.224	0.974	0.343
BMI, kg/m^2	CD	0.24	1.674	0.1
	CG	0.655	3.676	0.002
Visceral tissue	CD	0.054	0.361	0.72
	CG	0.535	2.688	0.015
BMR	CD	0.429	3.184	0.003
	CG	0.366	1.62	0.124

Significance at 95% level; R, correlation; T, *t*-value. Abbreviations: BMD, bone mineral density; BMI, body mass index; BMR, basal metabolic range.

Table 5. The results of the univariate linear regression model in the study and control group for L1-L4 BMD.

Variable	Group	R	T	*p*-Value
Body mass, kg	CD	0.475	3.664	<0.001
	CG	0.336	1.515	0.147
Fat tissue, kg	CD	0.191	1.307	0.2
	CG	0.319	1.428	0.17
Fat-free mass, kg	CD	0.462	3.498	0.001
	CG	0.186	0.802	0.434
Muscle mass, kg	CD	0.441	3.295	0.002
	CG	0.168	0.725	0.478
BMI, kg/m^2	CD	0.298	2.12	0.039
	CG	0.456	2.173	0.043
Visceral tissue	CD	0.136	0.913	0.366
	CG	0.406	1.888	0.075
BMR	CD	0.44	3.376	0.002
	CG	0.267	1.14	0.27

Significance at 95% level; R, correlation; T, *t*-value. Abbreviations: BMD, bone mineral density; BMI, body mass index; BMR, basal metabolic range.

4. Discussion

In our study, osteopenia was observed in the FN in 19.65% of the patients and in L1–L4 in 26.79% of the patients. A total of 1.79% of the patients—i.e., one patient—exhibited osteoporosis in the L1–L4 region, while 3.57% of the patients—i.e., two patients—displayed the disease in the FN.

A greater proportion of patients exhibited low BMD in the L1-L4 region than in the FN. Significant positive correlations were observed between BMD and anthropometric and

metabolic variables, including body weight, FFM, muscle mass, and BMR for both L1–L4 and the FN. Additionally, a significant positive correlation was observed between BMI and BMD of the L1–L4 region.

Similarly to us, Lewis et al. reported data on T-scores in the lumbar spine in comparison with the femoral neck. These researchers reported that osteoporosis at the hip affects 7% of patients and osteoporosis at the spine affects 14% of patients [17]. On the contrary, Ganji et al. reported no significant difference between decreased BMD in the femoral neck and the spine in CD: in a group of 76 CD patients aged 20–60 years old, 55% had osteopenia in the femoral neck or spine and 36% had osteoporosis in the femoral neck or spine [18]. The Polish study of premenopausal women and men with CD by Szymczak et al. showed a prevalence of osteopenia of 62.8% at the femoral neck and a prevalence of osteoporosis of 20% at the same site. Furthermore, the study indicated a prevalence of osteopenia in the lumbar spine of 57.2%, along with a prevalence of osteoporosis of 28.6% [19]. In 2019, Ganji et al. estimated in a systematic review comprising 563 premenopausal women and men that osteoporosis occurs in 14.4% and osteopenia in 39.6% of CD patients [20].

The etiology of osteoporosis in CD is multifactorial. It is hypothesized that bone alterations in CD patients primarily result from impaired intestinal absorption efficiency, which subsequently causes hypocalcemia and vitamin D malabsorption. Additionally, chronic inflammation results in an increased production of pro-inflammatory cytokines in the mucosa and serum, including TNF-α (tumor necrosis factor-α), IL-1 (interleukin-1), and IL-6 (interleukin-6), which disrupt bone growth and autoimmune factors [7,13]. The prevalence of osteopenia and osteoporosis is frequently inconsistent across studies. In evaluating these data, it is essential to consider the selection of patients included in the study group and the potential influence of other risk factors.

The findings of our study indicate that there are no statistically significant differences in body mass, BMI, fat tissue, muscle mass, and fat-free mass between the two groups. However, subjects with lower body weight, FFM, muscle mass, and BMR were more likely to have a diagnosed reduced BMD. The relationship between reduced body composition parameters and reduced BMD can be explained by the direct mechanical stimulation of bone by muscle, which promotes osteogenesis.

Furthermore, reduced muscle mass and osteoporosis share common pathophysiological pathways, gene polymorphisms, inflammatory status, or malnutrition [21,22]. It is noteworthy that our study also observed an association between low body mass and body fat content with a higher prevalence of reduced BMD. Furthermore, paracrine and endocrine communication involving osteocalcin, vascular endothelial growth factor, insulin-like growth factor-1, osteoglycin, fibroblast growth factor-2, and myostatin have been indicated and are collectively referred to as bone–muscle interaction [22,23].

It is noteworthy that our previous study demonstrated that individuals with CD exhibited lower body mass, BMI, FFM, and fat mass compared to the control group. This discrepancy may be attributed to the fact that this study included only women and did not impose an upper age limit. In the aforementioned study, the prevalence of reduced BMD was also markedly elevated, with 23.33% to 50% of patients with CD exhibiting osteopenia or osteoporosis, contingent on the measurement site.

The literature contains conflicting reports. Some studies indicate that patients, regardless of their adherence to a GFD, have lower body weight, BMI, BMD, bone mineral content, fat mass, and fat-free mass than controls [24]. In a study conducted by González et al., a cohort of women between the ages of 20 and 60 was observed. The women were either following or not following a GFD. It was found that women with CD had a lower BMI compared to the control group. Additionally, women with CD who were not following a GFD had a lower BMI than those who were on a GFD. Furthermore, they had a lower body fat mass and FFM than the control group [25]. It is important to note that CD is characterized by the presence of villous abnormalities, which in turn results in the malabsorption of both macronutrients and micronutrients. Moreover, a broad spectrum of gastrointestinal manifestations, such as diarrhea, can predispose one to decreased intestinal absorption [1].

However, it is paradoxical that there is an increasing prevalence of overweight individuals with CD, particularly in Western countries. A study conducted by Tucker et al. on a group of 187 adults with CD revealed that 44% of them were overweight (31%) or presented with obesity (13%). This indicates a shift in the profile of CD patients and a potential need for a more comprehensive approach to their care [26]. In our study, 14.2% (n = 8) of the patients had a BMI indicating overweight or obesity.

Furthermore, the results of the study conducted here indicated that 88% of the CD patients had supplemented their diets with vitamin D, while 24.49% had done so with calcium. Among the control group, only 38.89% reported vitamin D supplementation, and none reported calcium supplementation. The concentration of 25(OH)D in serum was observed to be higher in individuals with CD than in healthy controls. The results are inconsistent with the hypothesis that patients with CD have lower serum concentrations of 25(OH)D, which would predispose them to the development of osteoporosis. Conversely, serum calcium levels were markedly diminished in individuals with CD.

The high percentage of individuals supplementing with vitamin D may be attributed to the fact that the patients enrolled in this study were under outpatient care at our clinic, where the supplementation of vitamin D and, if necessary, calcium is recommended.

One of this study's principal strengths is the application of relatively rigorous exclusion criteria. To prevent overlap between secondary factors of osteoporosis and primary factors, individuals over the age of 50 and postmenopausal women were excluded from the study group. In addition, individuals with comorbidities that could potentially affect BMD and those currently or previously taking glucocorticosteroids were excluded from the study group.

A limitation of this study is the relatively small number of patients included in each group. Moreover, we did not specify the season of our study: due to variable exposure to sunlight, vitamin D concentrations could potentially be affected. We did not include information about physical activity. Furthermore, a total of 21.5% of patients with CD had been diagnosed less than one year before entering this study. In this cohort, bone mass may potentially improve following the introduction of a GFD.

Nevertheless, we are continuing to collect data and may be able to publish data on larger groups in the future. A further limitation is the lack of data on nutritional and genetic factors, which may have affected both BMD and the course of the disease. Accordingly, further comprehensive studies on these factors are necessary.

In conclusion, the findings of this study indicate that celiac disease patients with lower body mass, fat-free mass, muscle mass, body mass index, and basal metabolic rate are at an elevated risk of developing osteopenia and osteoporosis. Despite a higher incidence of osteopenia and osteoporosis in celiac patients, there are no significant differences in body composition between the two groups.

Adherence to a strict gluten-free diet is crucial for the prevention and management of bone mineral density. It has been demonstrated that adherence to a gluten-free diet has a beneficial impact on BMD in patients with celiac disease. This suggests that effective management of celiac disease would potentially reduce the elevated risk of fractures. It is important to note, however, that the mechanism of osteoporosis in patients with celiac disease is complex. On the one hand, villous atrophy impairs the efficiency of intestinal absorption, leading to hypocalcemia and vitamin D malabsorption. This in turn results in secondary hyperparathyroidism, as well as chronic inflammation, which causes an increase in the production of pro-inflammatory cytokines in the mucosa and serum, particularly TNF-α, IL-1, and IL-6. This disrupts bone growth and autoimmune factors [27].

Furthermore, there are data indicating that the quality of the diet of people with celiac disease is inferior to that of individuals on a traditional diet. Moreover, gluten-free products are often highly processed. In addition, a diet that is both balanced and rich in fiber and polyphenols plays an instrumental role in modulating the gut microbiota, which has been identified as a potential vital factor in bone metabolism. Furthermore, physical activity,

particularly resistance training, which enhances lean body mass, is a crucial element in preventing bone disorders in individuals with celiac disease [27].

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Data Availability Statement: The raw data supporting the conclusions of this article will be made available by the authors on request.

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