BODY COMPOSITION ALTERATIONS IN CELIAC DISEASE

PhD Thesis

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1. Introduction

1.1. Celiac disease

Celiac disease (CD) is a permanent T-cell-mediated enteropathy caused by the consumption of gluten - the major protein fraction of wheat, rye and barley - in genetically predisposed individuals. In most countries, the average prevalence of CD is about 1%. The only proven effective treatment for CD is a strict, lifelong gluten-free diet (GFD).

1.1.1. Pathomechanism of CD

Environmental factors (dietary gluten) and genetic predispositions are essential in the pathogenesis of CD.

Gluten is the collective name for the storage proteins (gliadins, glutenins) of wheat, rye, and barley. These gluten proteins trigger the adaptive immune response in CD. Gastric and pancreatic enzymes are not able to completely degrade these proteins - partly due to their unusual repetitive sequences - and this proteolytic stability is a key factor in their immunogenicity.

Individuals with a family history of CD have a 10-15% risk of developing the disease in their lifetime, and among identical twins, the risk of simultaneous occurrence is 50-75%. The major histocompatibility complex (MHC) class II genes are the most important genetic factors. The human leukocyte antigen (HLA)-DQ2 is present in about 90% of patients with CD with a few exceptions; the remaining patients are usually HLA-DQ8 carriers.

The composition of the bacterial mass in the gut has a fundamental impact on the immunological events in the gut. Higher prevalence of Bacteroides, Proteobacteria strains, and lower prevalence of Bifidobacterium and Lactobacillus strains were found in patients with CD. Changes in gut bacterial composition also affect gut permeability. Increased permeability also facilitates the development of the disease by allowing larger, immunogenic peptides to enter the lamina propria.

1.1.2. Clinical presentation and diagnosis of CD

CD is called a clinical chameleon and can present at any age with different manifestations. CD can be divided into classical, non-classical, and subclinical forms, depending on the clinical features presenting at diagnosis

In adults, the diagnosis of CD is based on a combined assessment of the clinical presentation, serological, and histological tests. Positive serology (immunoglobulin A [IgA] anti-tissue transglutaminase 2 antibody [anti-tTG2]) and villous atrophy provide a definitive diagnosis, while cases with discordant results require HLA testing. In children, duodenal biopsy can be omitted if certain conditions (a sufficiently high antibody titer) are satisfied.

1.2. Body composition

Body composition is the ratio of the individual components of the human body as a whole to each other or the total body weight. Analyzing body composition provides information on both the nutritional status and the functional capacity of the human body; useful for describing growth and development and understanding the causes of health and disease and has a key role in planning nutritional strategies and monitoring therapeutic interventions. Measuring human body composition is an objective method of assessing nutrition, which changes when the balance between nutrient intake and need is upset. With the increasing prevalence of obesity and lifestyle-related diseases, the need for more sensitive and accurate body composition measurement methods is becoming more urgent. Many techniques are available to assess body composition, ranging from simple indirect measurements to more sophisticated direct volumetric measurements.

1.2.1. Body composition and GFD

Several studies suggested a difference in body composition across untreated CD patients, treated CD patients, and non-celiac control subjects. Generally, most classical CD patients not adhering to a GFD are underweight and have lower body mass index (BMI), fat mass (FM), fat-free mass (FFM), and bone mass compared to a non-celiac control group. After introducing a GFD, the intestinal mucosa heals, the proinflammatory response ceases, and the absorption of nutrients is restored. These factors together can cause an increase in body weight, BMI, FM, FFM, and bone mass, which serves a potential explanation for the difference in body composition observed between treated CD patients and non-celiac controls, which remains undetected in a fraction of the cases. Lack of complete response can be due to dietary transgressions or failure to achieve mucosal healing, which is typical in cases diagnosed late in adulthood.

There are several publications on the quality of the GFD, which show that it is unbalanced and generally does not meet the requirements of a healthy diet, as it is high in energy, simple carbohydrates, fat and saturated fat, while low in complex carbohydrates, fibre, vitamins (B1, B2, B6, B9, D, E) and minerals (iron, calcium, potassium, zinc, manganese, iodine, selenium, magnesium). The nutritional composition of gluten-free products consumed as part of the diet is not always optimal. However, the nutritional profile of these products is generally less favourable than their gluten-containing counterparts: they are high in fat, saturated fat, simple carbohydrates (glucose syrup, rice flour, potato flour, corn flour) and low in fibre, protein, vitamins, and minerals. An unbalanced GFD combined with improved absorption may also be

responsible for undesirable changes in both body weight and body composition parameters (substantial gain in FM and a modest increase in FFM).

As a consequence of the reasons above, the result can be disproportionate body composition and metabolic alterations, including the frequent development of nutrition-related disorders, such as metabolic dysfunction-associated fatty liver disease (MAFLD). Moreover, CD patients who are overweight at diagnosis have a higher risk of cardiovascular (CV) events and developing metabolic alterations, compared to non-overweight CD patients.

The current guidelines propose no recommendations for baseline and follow-up body composition assessment. Body composition-related parameters, such as FM and FFM, should be evaluated to assess CD patients' nutritional status comprehensively and to monitor therapeutic response.

2. Objectives

I. Comparing the body composition of patients with CD with that of non-celiac individuals.

II. To investigate the effect of clinical indicators at diagnosis (clinical picture, histology, comorbidities, etc.) on the change in BMI following a GFD.

III. Examination of the effects of a GFD on body weight, BMI, and body composition.

The objectives were examined at different levels of evidence. First, a meta-analysis was conducted, followed by a retrospective cohort study.

3. Study I. – Meta-analysis and systematic review

3.1. Methods

To adapt the clinical question to meta-analysis, we used the PECO framework (P: population, E: exposure, C: control group, O: outcome). In our study, we investigated body composition (O) in selected celiac patients from the general population (P) before (E) and after at least one year of gluten-free diet (C1), compared to the body composition of the healthy population (C2). This systematic review and meta-analysis is reported in conformity with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Statement. The protocol of this study was registered under registration number CRD42021229522 in PROSPERO.

3.1.1. Data sources and search strategy

A systematic search was conducted using five major literature databases, including MEDLINE (via PubMed), Embase, Cochrane Register of Controlled Trials (CENTRAL), Web of Science and Scopus, from inception to 15 July 2021. We designed a search key, which contains terms associated with CD and body composition. In-built database filters were only applied in the

case of Scopus (Article title, Abstract, Keywords). Furthermore, reference lists of the relevant studies were manually screened for any additional studies. We did not contact the authors of the primary studies for further data.

3.1.2. Selection and eligibility

EndNote X9 software (Clarivate Analytics, Philadelphia, PA, USA) was used for record management. The generated database contained all relevant publications, which were first screened for duplicates. The remaining publications were then subjected to a three-step selection process (title, abstract, then full paper), carried out independently by two authors, with any discrepancies resolved by a third investigator. Cohen's kappa coefficient (κ) was calculated to measure the reliability of agreements during the selection process. Human studies (cohort, case-control, and cross-sectional), both full-texts and conference abstracts, that reported on at least one of the pre-specified outcomes were eligible for inclusion. We only included studies in which three comparisons were reported: (1) Newly diagnosed CD patients vs. non-celiac control subjects, (2) CD patients at the time of the diagnosis vs. the same patients after at least a one-year GFD, (3) CD patients after at least a one-year GFD vs. non-celiac control subjects. To be included, the diagnosis of CD had to be based on serological testing and intestinal biopsy or according to the recommendations of the pediatric guidelines. Study populations with further selection (e.g., diabetic CD patients only, women only) were excluded. Studies recruiting patients from specific age groups were included. Study participants had to follow either a regular gluten-containing diet or a traditional GFD. Studies with further dietary modifications (e.g., a low-carb GFD, a GFD with vitamin B12 supplementation) were excluded. If a non-celiac control group was recruited, control subjects had to be declared to be healthy; otherwise, the study was excluded (the recruitment of, e.g., "other gastrointestinal patients" or "patients with negative endoscopy results" was not accepted).

3.1.3. Data extraction and risk of bias assessment

We designed separate forms for each comparison of groups. The following parameters were collected: General characteristics of the study (authors, title, year of publication, study design), description of the population (sample size, age (years), gender, BW (kg or Z-score), body height (cm or Z-score), BMI (kg/m2 or Z-score)), diagnostic method of CD, follow-up period and the outcomes including FM (kg or % or Z-score), FFM (kg or % or Z-score), visceral fat area (cm2), total body water (% or Z-score), bone mineral content (BMC) (g or Z-score) and bone mineral density (BMD) (g/cm2 or Z-score). The year of publication and study sites were compared to identify overlapping populations.

Bias assessment of the studies included was performed by applying the NIH "Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies" guidelines, which assesses measures against selection bias, information bias and confounding effects.

3.1.4. Statistical analysis

For meta-analytical calculations, we used means and standard deviations collected from the studies. In meta-analyses, pooled weighted mean differences (WMDs) with 95% confidence intervals (CIs) were calculated. The DerSimonian and Laird random-effects model was applied. Cochrane's Q and the I^2 statistics were used to quantify heterogeneity. Forest plots were used to visually display the results of the meta-analysis. Due to the low number of studies, publication bias was not tested. The analysis was performed with STATA software version 15 (Stata, College Station, Texas).

3.2. Results

3.2.1. Search and selection

A total of 3013 records were identified from the electronic databases. After the automatic and manual removal of duplicates, 1554 records remained. After screening by title and abstracts, 65 studies were screened for eligibility; 25 of which were included in the systematic review, and seven of which were eligible for meta-analysis.

3.2.2. Results of meta-analysis

Three studies evaluated FM of CD patients at the diagnosis and after at least a one-year follow-up on GFD. The one-year-long GFD treatment resulted in a statistically significant increase in FM (WMD = 4.1 kg, 95% CI = 1.5 to 6.6, I2 = 75.8%, p = 0.016) (Figure 1). The amount of data did not allow us to perform a meta-analysis on FFM; however, in most of the studies, the change during a GFD was not significant.

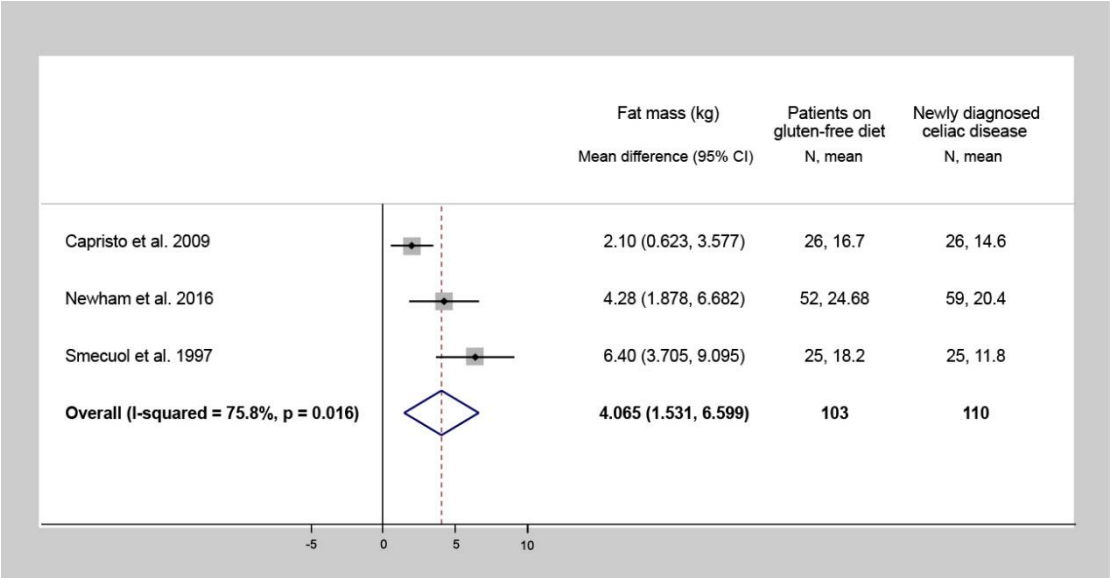

Figure 1. Forest plot of studies comparing fat mass of celiac disease patients after at least a one-year gluten-free diet to that of the same patients at diagnosis (a positive number indicates a gain in fat mass following a gluten-free diet). N: number of patients.

Four studies investigated the difference of FM and FFM values between CD patients following a one-year-long GFD and control subjects. Among CD patients on a GFD for at least one year, lower FM (WMD = −5.8 kg, 95% CI = −8.7 to −2.9, I2 = 50.1%, p = 0.135) (Figure 2) and FFM (WMD = −1.9 kg, 95% CI = −3.0 to −0.7, I2 = 0.0%, p = 0.414) (Figure 3) were detected, compared to the control group.

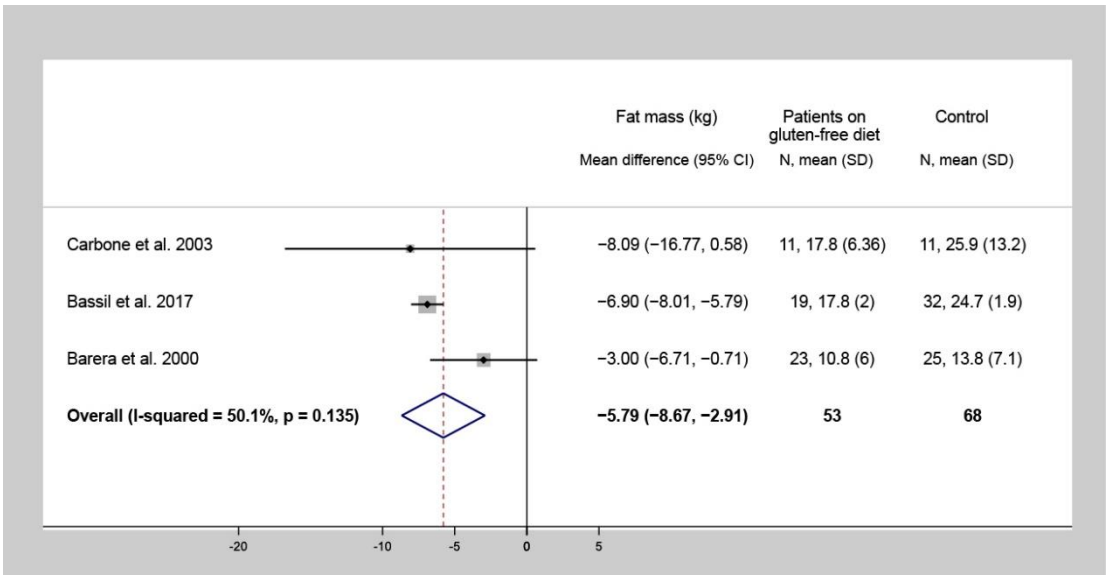

Figure 2. Forest plot of studies comparing fat mass of celiac disease patients on a gluten-free diet for at least one year to that of non-celiac control subjects (a negative number indicates a lower fat mass of the celiac population compared to controls). N: number of patients.

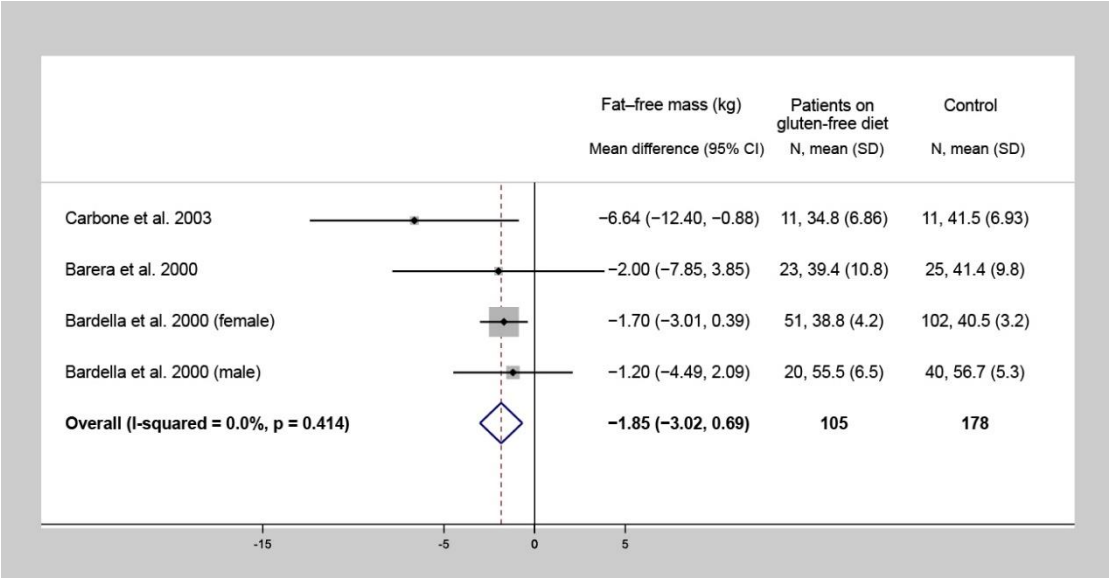

Figure 3. Forest plot of studies comparing fat-free mass of celiac disease patients on a gluten-free diet for at least one year to that of non-celiac control subjects (a negative number indicates a lower fat-free mass of the celiac population compared to controls). N: number of patients.

3.3. Discussion

In this study, we aimed to compare the body composition across CD patients before a GFD, CD patients after a one-year GFD, and non-celiac control subjects. While the difference in body composition between newly diagnosed CD patients and non-celiac control subjects could not be meta-analyzed due to the diversity in data, we observed that BW, BMI, FM, FFM, BMC and BMD values were lower in CD patients than in the non-celiac control group in most of the studies. This can be attributed to malabsorption, the classical clinical presentation of CD. Consequently, the indicators of the nutritional status of newly diagnosed CD patients on a gluten-containing diet are usually worse than those observed in the average population. Most studies that evaluated changes in body composition between CD patients at the time of the diagnosis and the same patients after at least a one-year follow-up period introduced a GFD as a BW, BMI, and FM promoter. Restored intestinal absorption and the unbalanced composition of a GFD, being rich in simple carbohydrates and saturated fats, resulted in weight gain. A GFD induced BW gain; hence, BMI improvement can be considered optimal when the FFM ratio is higher than the FM; however, not among most of the CD patients. Our meta-analysis showed the same phenomenon, as we detected a significant increase in FM, but FFM mostly did not change during a one-year GFD. Although, after three or five years of diet, FFM tended to rise. In contrast, the study by Rocco et al. assessed body composition at diagnosis and after at least 12 months of GFD and BMI plus FM did not change during the diet. However, the decreased FFM influenced the FM/FFM ratio unfavorably. This means that BW and FM (thus fat deposits)

may recover easily, contrasting FFM, which is unable to normalize rapidly (≈one year). The disproportionate increase in FM is not desirable in CD patients who have normal body weight or are overweight at diagnosis.

Our meta-analysis on the changes of FM and FFM showed that these parameters do not reach the level of the non-celiac control population after a one-year GFD, corroborating previous findings. The reason could be poor dietary adherence, incomplete mucosal recovery, and a lack of awareness about disease management. While most of the studies included CD patients who had satisfactory compliance with a GFD, the degree of dietary adherence can range from partial to strict. Smecuol et al. and Wiech et al. reported that the improvement in body composition is more substantial in the case of a strict GFD; however, in another study, the dietary adherence did not influence the nutritional status. The heterogeneous nature of CD and the different national and cultural aspects of dietary habits could lead to further diversity. In children, it is hard to distinguish between the effect of the diet and the normal growth on body composition, so that data from longitudinal, follow-up studies of different age groups (under 18 years) are barely comparable. For this reason, data on adults and children should be analyzed separately. Unfortunately, we could only perform meta-analysis relying on adult patients' data. Regarding other body composition parameters, BMC was lower in newly diagnosed CD patients than in controls. After at least one year of GFD treatment, BMC tended to normalize and, in the long-term (>one year), it restored completely compared to control subjects.

BMD of patients who started a GFD in childhood was higher than that of patients first diagnosed in adulthood, indicating that the earlier the diagnosis, the better the clinical outcomes. Among the 25 studies, only one measured visceral fat area. The researchers observed a statistically not significant but measurable increase in the visceral fat area among treated CD patients, compared to controls. Moreover, the visceral fat area of 40% of CD patients on a GFD was above 100 cm^2, indicating elevated risk for adverse metabolic alterations. Four studies evaluated the effect of CD and GFD on total body water in children, yielding inconsistent findings. Abnormal body composition of CD patients as well as changes in body composition during a GFD and the assessment of nutritional status at the diagnosis of CD and during regular follow-up visits are worth considering. Information about body composition helps the early detection of malnutrition at diagnosis and supports the prevention of long-term complications of macro- and micronutrient deficiencies (e.g., short stature, osteoporosis). Several studies suggested that the earlier the diagnosis, the better the nutrition education and consequently, the body composition is expected to recover. However, a complete recovery is more likely to occur in childhood rather than in adulthood. Previous findings supported the tendency that non-classical and silent forms

of CD are becoming more frequent, and the proportion of patients with a normal or high body weight at diagnosis is increasing rapidly. The improvement of nutritional status was also observed both at the presentation of CD and after a GFD. These data requests the management of the consequences of both the under- and overnourishment in the care of CD patients. A personalized diet and the promotion of a healthy diet and lifestyle are expected to trigger favorable trends in the changes of body composition

3.4. Conclusions

The body composition of CD patients differs from that of the non-celiac population. A GFD was associated with a substantial gain in FM and a modest increase in FFM; however, even after a longstanding GFD, these parameters did not reach the optimal. Current CD guidelines do not recommend baseline and follow-up body composition assessments. The findings of our review suggest that follow-up of the nutritional status in addition to body composition measurements and personalized dietary counseling, are important to prevent the long-term consequences of malnutrition and disproportionate weight gain. Prospective, well-designed studies recruiting a sufficient number of CD patients investigating body composition and its changes during a GFD are awaited.

4. Study II. - Cohort study

4.1. Study Population and methods

In this study, we investigated the associations of BMI at diagnosis of CD and during the GFD, with a special focus on its clinical presentation. This study is reported in conformity with the Strengthening the Reporting of Observational studies in Epidemiology (STROBE) Statement. The study is conducted in full accordance with the Declaration of Helsinki and is approved by the Regional and Local Research Ethics Committee of the University of Pécs, Pécs, Hungary (Ref. No. 6918).

4.1.1. Study population and eligibility

This single-centered, retrospective cohort study involves patients from our tertiary center enrolled and admitted at the University of Pécs (Pécs, Hungary). Patients were eligible for inclusion if they were diagnosed with CD in adulthood (≥18 years of age) and their BMI at diagnosis and during follow-up was available. All CD patients following diagnosis - verified by a gastroenterologist based on the combination of clinical, serological, and histopathological data as per the currently valid guidelines - were instructed to follow a GFD.

4.1.2. Data extraction

Data were extracted by using paper-based medical files and the current medical software, eMedSolution, based on disease identifiers. The period for paper-based and electronic data

collection begins with the years of 1992 and 2007, respectively, and concludes in 2022. Data of all eligible patients were manually retrieved by investigators with a healthcare degree into a pre-defined data collection table. Next, all data points were verified by a third investigator, also with a medical degree.

The following parameters were collected: gender, age upon diagnosis, calendar year of diagnosis of CD, clinical presentation (classical or non-classical CD by the Oslo Classification), histology and serological results (anti-tissue transglutaminase (tTG) IgA and IgG, anti-endomysial antibody (EMA) IgA and IgG), the presence of IgA deficiency, anemia, osteoporosis, dermatitis herpetiformis, body height (m) and body weight (kg) upon diagnosis of CD, and body weight (kg) 1–15 years following diagnosis of CD.

4.1.3. Statistical analysis

An expert biostatistician performed the analyses using the software IBM SPSS Statistics 28 (IBM Corporation, Armonk, NY, USA).

Patients were allocated into three groups by length of follow-up: short- (1–2 years), intermediate- (3–5 years), and long-term follow-up (6–15 years), corresponding to the length of the GFD. Variables of interest were analyzed across these groups.

Continuous variables were expressed as mean ± standard deviation if they showed a normal distribution, verified by the Kolmogorov–Smirnov test. In support of comparative analysis, with normal distribution, the independent t-test, the ANOVA test with Tukey's HSD post hoc test, and the Repeated Measures ANOVA test were used. Regarding comparative analysis, with non-normal distribution, the non-parametric tests as the Mann–Whitney U-test and the Friedman test were used.

Categorical variables were expressed as relative frequencies. The data were analyzed using contingency tables and the Chi-squared or Fisher's test, as appropriate.

Statistical significance was established as a p-value of < 0.05.

4.2. Results

A total of 192 CD patients were included in the study. Characteristics of the patients included are summarized in Table1. Mean age upon diagnosis of CD was 37.5 ± 13.2 years (range: 18.0–70.0 years), and approximately three-fourths of patients were females. Out of the 192 subjects, 101 (52.6%) had classical CD. The mean BMI of the study population was 21.7 ± 4.3 kg/m^2. Roughly half (50.5%) of the patients had normal body weight at diagnosis, followed by underweight and overweight classes. Most of the patients had normal IgA levels, no anemia, and no osteoporosis or dermatitis herpetiformis upon diagnosis.

Table 1. Characteristics of patients included.

Variable	Total cohort of patients	Patients with classical CD	Patients with non-classical CD	*p*-value (classical vs. non-classical CD)
Age at diagnosis	**N=192**	**N=101**	**N=91**	
Mean ± standard deviation, years	37.5±13.2	37.9±14.1	37.0±12.1	*0.638*
Gender	**N=192**	**N=101**	**N=91**	
Males	43 (22.4%)	21 (48.8 %)	22 (51.2%)	*0.574*
Females	149 (77.6%)	80 (53.7 %)	69 (46.3 %)	
BMI at diagnosis	**N=192**	**N=101**	**N=91**	
Mean ± standard deviation, kg/m^2	21.7±4.3	20.7±4.4	22.9±4.0	*<0.001**
Underweight	52 (27.1%)	40 (39.6%)	12 (13.2%)	*<0.001**
Normal	97 (50.5%)	45 (44.6%)	52 (57.1%)	
Overweight	33 (17.2%)	11 (10.9%)	22 (24.2%)	
Obesity class I.	9 (4.7%)	4 (4.0%)	5 (5.5%)	
Obesity class II.	1 (0.5%)	1 (1.0%)	0 (0.0%)	
Obesity class III.	0 (0.0%)	0 (0.0%)	0 (0.0%)	
Histology at diagnosis	**N=129**	**N=70**	**N=59**	
Marsh 1-2	6 (4.7%)	3 (50.0%)	3 (50.0%)	*0.718*
Marsh 3a-3b	54 (41.9%)	27 (50.0%)	27 (50.0%)	
Marsh 3c	69 (53.5%)	40 (58.0%)	29 (42.0%)	
tTG IgA at diagnosis	**N=172**	**N=89**	**N=83**	
Negative	12 (7.0%)	6 (50.0%)	6 (50.0%)	*0.948*
Low positive	58 (33.7%)	31 (53.4%)	27 (46.6%)	
High positive	102 (59.3%)	52 (51.0%)	50 (49.0%)	
tTG IgG at diagnosis	**N=158**	**N=80**	**N=78**	
Negative	66 (41.8%)	32 (48.5%)	34 (51.5%)	*0.878*
Low positive	68 (43.0%)	35 (51.5%)	33 (48.5%)	
High positive	24 (15.2%)	13 (54.2%)	11 (45.8%)	
EMA IgA at diagnosis	**N=142**	**N=69**	**N=73**	
Negative	19 (13.0%)	9 (47.4%)	10 (52.6%)	*0.619*
Weak positive	13 (9.2%)	8 (61.5%)	5 (38.5%)	
Strong positive	110 (77.5%)	52 (47.3%)	58 (52.7%)	
EMA IgG at diagnosis	**N=95**	**N=47**	**N=48**	
Negative	35 (36.8%)	20 (57.1%)	15 (42.9%)	*0.520*
Weak positive	8 (8.4%)	4 (50.0%)	4 (50.0%)	
Strong positive	52 (54.7%)	23 (44.2%)	29 (55.8%)	
IgA deficiency at diagnosis	**N=92**	**N=44**	**N=48**	
No	86 (93.5%)	41 (47.7%)	45 (52.3%)	*1.000*
Yes	6 (6.5%)	3 (50.0%)	3 (50.0%)	
Anemia at diagnosis	**N=187**	**N=99**	**N=88**	
No	105 (56.1%)	51 (48.6%)	54 (51.4%)	*0.176*
Yes	82 (43.9%)	48 (58.5%)	34 (41.5%)	
Bone mineral density at diagnosis	**N=110**	**N=63**	**N=47**	
No	47 (42.7%)	25 (53.2%)	22 (46.8%)	*0.184*
Osteopenia	32 (29.1%)	16 (50.0%)	16 (50.0%)	
Osteoporosis	31 (28.2%)	22 (71.0%)	9 (29.0%)	
Dermatitis herpetiformis at diagnosis	**N=192**	**N=101**	**N=91**	
No	166 (86.5%)	92 (55.4%)	74 (44.6%)	*0.048**
Yes	26 (13.5%)	9 (34.6%)	14 (65.4%)	

N: number of patients; tTG: anti-tissue transglutaminase antibody; EMA: anti-endomysial anti-body; BMI: body mass index; * indicates statistical significance. Dichotomous variables are ex-pressed in number of patients and percentage of total.

4.2.1. Clinical variables and mean BMI at diagnosis of CD

In terms of gender, males had significantly higher mean BMI upon diagnosis of CD than when compared with females (22.9 ± 4.1 vs. 21.4 ± 4.3 kg/m^2, respectively, $p = 0.041$).

Concerning anthropometric parameters, non-classical CD patients had significantly higher mean BMI upon diagnosis than when compared with classical CD patients ($p < 0.001$). Most of classical and non-classical CD patients belonged to the normal BMI class. The proportion of underweight patients was significantly lower, and the proportion of overweight patients was significantly higher in non-classical cases than classical CD ($p < 0.001$ for both) (Table 1).

Mean BMI upon diagnosis of CD was significantly associated with the tTG IgG titer category ($p = 0.024$), meaning those patients with high positive tTG IgG titers had significantly lower mean BMI, when compared to patients with negative titers (20.2 ± 3.4 vs. 22.9 ± 4.7 kg/m^2, respectively, $p = 0.026$).

Mean BMI upon diagnosis of CD did not significantly differ by other variables, including serological results (tTG IgA, EMA titers), histology, IgA deficiency, anemia, osteoporosis, and dermatitis herpetiformis at diagnosis ($p > 0.05$ for all comparisons).

4.2.2. Clinical variables and BMI classes at diagnosis of CD

Factors significantly associated with the BMI class at a diagnosis of CD are presented in Table 2.

Table 2. Factors significantly associated with BMI class at diagnosis of CD.

Variable		Total number of patients	BMI class at diagnosis						*p*-value
			Underweight	Normal weight	Overweight	Obesity class I.	Obesity class II.	Obesity class III.	
Gender	Males	43	7 (16.3%)	19 (44.2%)	15 (34.9%)	2 (4.7%)	0 (0.0%)	0 (0.0%)	*0.010**
	Females	149	45 (30.2%)	78 (52.3%)	18 (12.1%)	7 (4.7%)	1 (0.7%)	0 (0.0%)	
Clinical presentation	Classical	101	40 (39.6%)	45 (44.6%)	11 (10.9%)	4 (4.0%)	1 (1.0%)	0 (0.0%)	*<0.001**
	Non-classical	91	12 (13.2%)	52 (57.1%)	22 (24.2%)	5 (5.5%)	0 (0.0%)	0 (0.0%)	
Anemia	No	105	21 (20.0%)	58 (55.2%)	22 (21.0%)	3 (2.9%)	1 (1.0%)	0 (0.0%)	*0.035**
	Yes	82	30 (36.6%)	37 (45.1%)	10 (12.2%)	5 (6.1%)	0 (0.0%)	0 (0.0%)	

BMI: body mass index; EMA: anti-endomysial antibody; * presented: significant result; values are reported in relative frequency and percentage.

Concerning gender, a significant difference was observed in the underweight and overweight classes: males were more likely to be overweight than when compared with females (34.9% vs. 12.1%), whereas females were more likely to be underweight than males (30.2% vs. 16.3%) ($p = 0.010$ for interaction).

There was a statistically significant association between clinical presentation and BMI class ($p < 0.001$ for interaction). As expected, the proportion of underweight patients was higher with classical CD compared to non-classical CD (39.6% vs. 13.2%, respectively), whereas overweight patients were more likely to have non-classical CD (24.2% vs. 10.9%, respectively).

Those who had anemia tended to be underweight (36.6% of the cases), whereas among those without anemia, only 20.0% of patients were underweight. In contrast, the proportion of overweight patients was higher in patients without anemia, compared to those with anemia (21.0% vs. 12.2%, respectively). There was a significant association between the BMI class and presence of anemia ($p = 0.035$ for interaction).

Data on IgA deficiency, serology, histology, osteoporosis, and dermatitis herpetiformis at diagnosis of CD did not significantly differ across BMI classes ($p > 0.05$ for all comparisons).

4.2.3. Mean BMI change during follow-up

As illustrated in Figure 4, the mean BMI at short-, intermediate-, and long-term follow-ups was significantly higher than when calculated at diagnosis ($p < 0.001$ for all comparisons).

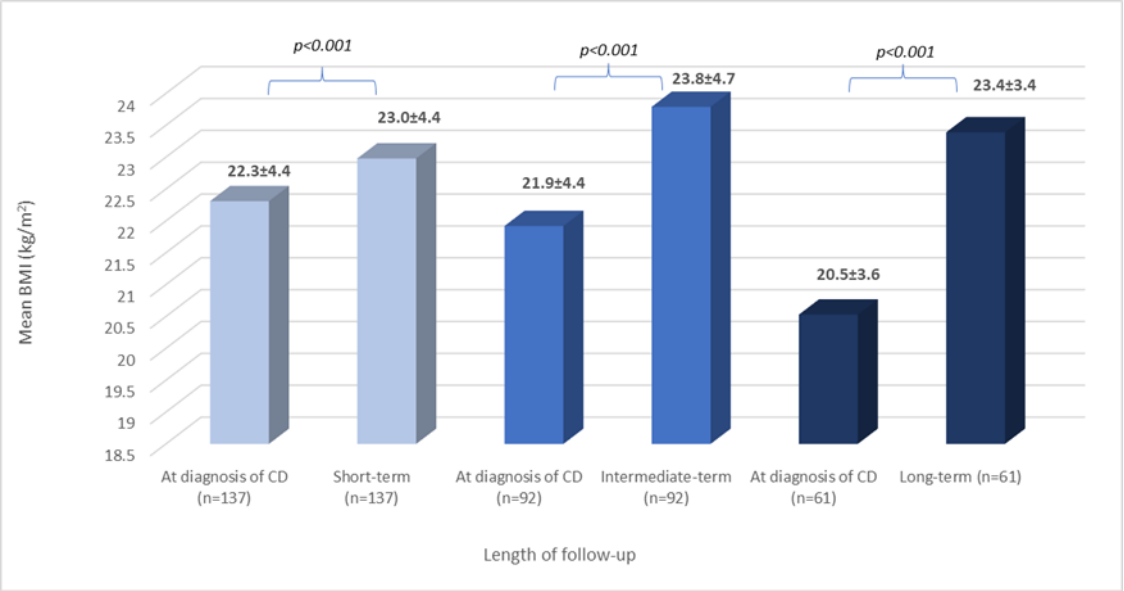

Figure 2. BMI change during follow-up: all patients. BMI: body mass index; CD: celiac disease; n: number of patients; values are reported in mean and standard deviation: x ± SD.

Out of the 192 patients, only 17 had available BMI data for each time frame of follow-up. Mean BMI increased significantly at short-term follow-up ($p = 0.034$), and BMI continued to rise during both intermediate- and long-term follow-ups, but only moderately ($p > 0.05$ for both). When comparing mean BMI at diagnosis to those calculated during follow-up, a significantly higher BMI was detected in all comparisons (Figure 5).

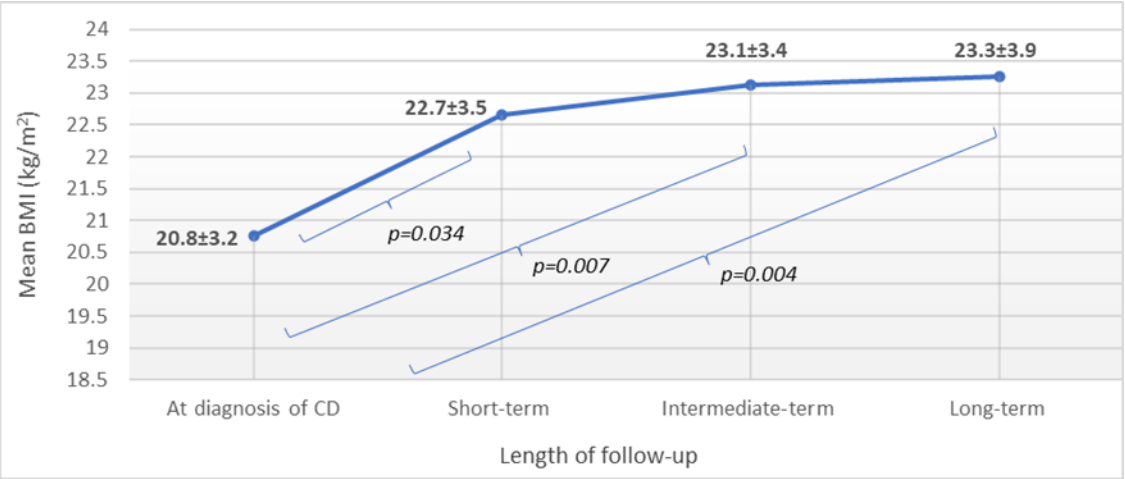

Figure 5. BMI change during follow-up: patients having available data for all time frames (n=17). n: number of patients; BMI: body mass index; CD: celiac disease; values are reported in mean and standard deviation: x ± SD.

4.2.4. BMI class change during follow-up

Out of the 192 patients, only 17 had BMI classes for each time frame. The Friedman test showed a significant difference between the groups ($p < 0.001$). In pairwise comparisons, the proportion of higher BMI classes increased during follow-up ($p = 0.034$ for the comparisons of BMI at diagnosis of CD vs. that at intermediate- and long-term follow-ups).

4.2.5. Association of BMI during follow-up with clinical variables

Males had a significantly higher mean BMI than females at all time frames ($p = 0.031$, $p = 0.029$, and $p = 0.033$ for short-, intermediate-, and long-term follow-ups, respectively).

In comparing the mean BMI of different time intervals, they differ significantly from BMI upon diagnosis in both males and females (Table 3).

Table 3. BMI within genders during follow-up.

Length of follow-up	Gender	N	Mean BMI (kg/m^2)	*p*-value
At diagnosis of CD	males	29	23.1±4.1	*0.042**
Short-term follow-up			24.5±4.3	
At diagnosis of CD		25	23.4±4.0	*0.001**
Intermediate-term follow-up			25.5±4.6	
At diagnosis of CD		9	22.4±4.1	*0.015**
Long-term follow-up			25.6±2.3	
At diagnosis of CD	females	108	21.9±4.4	*0.001**
Short-term follow up			22.6±4.3	
At diagnosis of CD		67	21.4±4.4	*<0.001**
Intermediate-term follow-up			23.1±4.6	
At diagnosis of CD		52	20.2±3.4	*<0.001**
Long-term follow-up			23.0±3.4	

N: number of patients; BMI: body mass index; CD: celiac disease; values are reported in mean and standard deviation: x ± SD; * presented: significant result.

Males upon diagnosis vs. those at short-term (Table 3) and short- vs. those at intermediate-term (n = 16, 25.5 ± 4.5 vs. 26.7 ± 4.8 kg/m^2, respectively, $p = 0.002$) had a significantly lower mean BMI; however, intermediate- vs. long-term comparisons did not yield a statistically significant

difference. In females, a statistically significant difference in mean BMI was observed only upon diagnosis vs. those at short-term follow-up (Table 3); however short- vs. intermediate-term and intermediate- vs. long-term comparisons did not yield a statistically significant difference.

Considering the association between clinical presentation and BMI, the significant difference observed at diagnosis was not detectable at short- and intermediate-term follow-ups; however, at the long-term follow-up, patients with non-classical CD (n = 25) had a higher BMI, compared to those with classical CD (n = 36) (24.5 ± 3.2 vs. 22.6 ± 3.4 kg/m^2, respectively, p = 0.039).

When comparing BMI change (from the diagnosis of CD) by clinical presentation, there was a significant difference between classical and non-classical CD patients at all time frames (Table 4).

Table 4. BMI change by clinical presentation of CD.

Length of follow-up	Clinical presentation	N	Mean BMI change (kg/m^2)	*p*-value
Short-term follow-up	classical	64	+ 1.1±2.3	*0.029**
	non-classical	73	+ 0.3±1.7	
Intermediate-term follow-up	classical	48	+ 2.9±3.4	*<0.001**
	non-classical	44	+ 0.7±2.4	
Long-term follow-up	classical	36	+ 3.6±2.8	*0.007**
	non-classical	25	+ 1.8±2.0	

N: number of patients; BMI: body mass index; + indicate the increase in BMI; values are report-ed in mean and standard deviation: x ± SD; ***** presented: significant result.

Regarding serology upon diagnosis of CD, significant short-term BMI change was detected between the tTG IgA titer groups (p = 0.005) and tTG IgG titer (p = 0.038) groups for CD patients. Concerning tTG IgA, a significantly higher BMI change was observed between cases with low positive and high positive titer (p = 0.008) when compared to those with negative vs. low positive and negative vs. high positive titer. Concerning tTG IgG, cases with negative vs. low positive titer had a significantly higher BMI change (p = 0.033), compared to those with negative vs. high positive and low positive vs. high positive titer. Upon intermediate- and long-term follow-ups, there was no significant association between BMI change and serology.

Data on other examined variables were not significantly associated with BMI change.

4.3. Discussion

CD is a potential cause of malnutrition since it is characterized by intestinal villous atrophy, leading to malabsorption. In typical cases, CD patients are malnourished and exhibit deficiency symptoms. However, a proportion of patients - despite the presence of villous atrophy - have no clinical signs and laboratory abnormalities relating to malabsorption or have only isolated abnormalities (e.g., anemia). These patients are typically recognized by extraintestinal manifestations of the disease (e.g., dermatitis herpetiformis, osteoporosis, or liver function test abnormalities). With the improvement of diagnostics and disease awareness, the fraction of

non-classical CD cases is increasing, and today, it has become more prevalent than the classical forms. According to our previous study, this trend is also observed among our CD patients; whereas, in the present study, the classical presentation of CD was slightly more frequent (52.6%).

A recent review found all anthropometric parameters to be worse in untreated CD patients when compared to controls. Depending on geographical regions, considerable differences exist in the proportion of under- and overweight CD patients. In an Indian study, the proportion of underweight CD patients was 36.2%, contrasting with an Italian and a Finnish study, in which it was only 6% and 4%, respectively. According to a study originating in the US, the mean BMI among classical CD patients was relatively high (24.4 kg/m^2), yet those of non-classical cases was even higher (25.7 kg/m^2). This tendency is supported by another study from the US, in which nearly half of the CD patients were already obese (BMI >30 kg/m^2) upon diagnosis, and the prevalence of obesity continued to rise linearly over the 5-year study span between 2014 and 2018. The prevalence of obesity is increasing worldwide, and this tendency is also true among CD patients. Tucker et al. demonstrated that 44% of CD patients were overweight and 13% were obese upon diagnosis, and, over the years of the GFD, the proportion of both classes increased steadily. A Chilean retrospective study reported similar results: the later the calendar year of diagnosis, the better the nutritional status and the higher the proportion of obese CD patients.

In our study, the proportion of underweight patients upon diagnosis was relatively high (27.1%), which can be partially explained by the predominance of classical CD cases. A significant difference was observed by gender: although the most common BMI class was the normal in both genders, in which a vast proportion of the females were underweight, males tended to be overweight. This difference can only partially be explained by the more common presence of the classical presentation among females (53.7% vs. 48.8%) than males. What is more important is that males had a prominent rise in BMI at the intermediate time frame of follow-up, moving them from the normal to the overweight class. This change is unfavorable from several points of view: it further increases the already high CV risk in aging males and - especially when combined with alcohol consumption - exacerbates the risk of developing fatty liver disease.

The association of clinical presentation and other diagnostic features of CD with BMI has not been previously studied. In our study, CD patients with classical presentation and high positive tTG IgG titers had a significantly lower BMI upon diagnosis than non-classical cases. Data on BMI at diagnosis did not significantly differ by IgA deficiency, other serological results (tTG

IgA, EMA titers), histology, anemia osteoporosis, and dermatitis herpetiformis upon diagnosis. In consideration of BMI classes upon diagnosis, patients with anemia tended to be underweight (36.6%), whereas a significant fraction of patients without anemia were overweight (21.1%). The context of a low BMI upon diagnosis with classical symptoms and high antibody titers is not surprising: a more prominent immune response assumes more severe mucosal damage and malabsorption.

Based on recent reviews, following a GFD resulted in generally improved nutritional status and significantly increased BMI. Our study supports this, showing the extent of BMI changes was significantly higher among patients with classical CD following a GFD in short-, intermediate-, and long-term follow-ups and in the short-term for both those with high tTG IgA and tTG IgG titers. The reason may be that patients with severe malabsorption and high antibody counts showed the most marked improvement in absorption due to the diet, since they had to catch up to normal nutritional status.

Weight gain due to the GFD is desirable for some patients but not always beneficial for others. Several studies draw attention to GFD-induced weight gain, which was associated with disproportionate body composition, as it resulted in a substantial gain in FM and a modest increase in FFM. In an Irish study, during a 2-year follow-up, weight gain occurred in 81%, whereas those who were initially overweight continued to gain weight, and the proportion of overweight individuals increased from 26% to 51%. Another retrospective study from Israel among adult CD patients reported the BMI among individuals following a GFD significantly increased, hence the proportion of overweight/obese (BMI $\geq$25 kg/m^2) patients rose from 32% to 38.8%. Probably, the composition of gluten-free products is generally less favorable than their gluten-containing counterparts since it has high calorie, saturated fat, simple carbohydrate, and sugar syrup contents.

The metabolic consequences of increased body weight and FM are most likely to occur in patients who are not underweight upon diagnosis of CD. The increased incidence of fatty liver disease in CD has been demonstrated by several studies. Surprisingly, the prevalence of fatty liver disease is already higher in untreated CD patients compared to the general population (hazard ratio (HR): 2.8, 95% CI 2.0–3.8). The risk of increasing in the first year following CD diagnosis was 13.3 (95% CI 3.5–50.3) but remained significantly elevated even beyond 15 years following the diagnosis of CD (HR = 2.5; 95% CI 1.0–5.9). Tortora et al. presented that the proportion of metabolic syndrome among newly diagnosed CD patients was 2%, rising to 30% following 1 year of a GFD. The association between CD and fatty liver disease may be due to increased permeability of the intestinal mucosa ("leaky gut") and a small intestinal bowel

overgrowth caused by dysbiosis. A malfunction of the gut-liver axis allows endotoxins and other microbial products to enter the bloodstream more quickly. Endotoxin influxes, such as lipopolysaccharides, trigger inflammatory reactions when they reach the liver and promote liver inflammation, fat accumulation, and fibrosis. Impaired permeability and altered microbiome are crucial factors in the development and progression of fatty liver.

A GFD can also alter energy expenditure and metabolism, possibly through changes in thyroid function or other hormonal pathways, which can further increase weight gain and metabolic stress on the liver, contributing to the development of MAFLD. Even on a GFD, individuals with CD may develop ongoing systemic inflammation due to dysregulation of the immune system. This may be associated with elevated levels of inflammatory cytokines and immune cell activation. Chronic systemic inflammation perpetuates liver inflammation and fibrosis, contributing to the progression of MAFLD.

High intakes of saturated and trans fats in a gluten-free diet can lead to increased liver fat accumulation. Stored triglycerides can cause lipotoxicity, leading to liver cell damage and inflammation, contributing to liver fibrosis. High-glycemic index foods consumed in the context of a GFD result in a rapid rise in plasma glucose levels, induce hyperinsulinaemia, promote hepatic lipogenesis, and inhibit fatty acid oxidation.

4.4. Conclusions

In our study, the proportion of underweight patients upon diagnosis was relatively high, especially in females. For these patients, the main challenge remains the elimination of malnutrition and the improvement of the nutritional status. According to our results, the BMI upon diagnosis was significantly higher in males and in patients with a non-classical phenotype. Although the mean BMI was within the normal range before and after a GFD, the mean BMI already increased significantly on the short-term follow-up. The significant difference in mean BMI observed upon diagnosis between classical and non-classical cases disappeared in the short-term with a “catch-up weight gain” in the classical group, however in the long-term, a significant difference was observed again with a BMI increase in the non-classical group. The number of the underweight patients tended to decrease with time during a GFD, and even in the short-term, the number of the overweight, mainly affecting males and non-classical cases, increased in the long-term. For the management of obesity-related problems, CV and metabolic consequences are new challenges in CD patient care. Nevertheless, dietary counseling and regular monitoring play important roles in ensuring adverse effects of a GFD do not prevail and weight gain is proportionate, as primarily FFM and not FM increases, and these interventions should particularly focus on non-classical cases and males.

5. Summary of findings

- Our meta-analysis confirmed that the body composition of patients with CD differs from that of individuals without CD.
- Body composition indicators do not become optimal even with a long-term GFD.
- In patients with CD, a GFD leads to a significant increase in FM, while the increase in FFM is more moderate. This leads to an unfavourable body composition with metabolic and CV consequences.
- In our retrospective cohort study, BMI at diagnosis is significantly higher in men and patients with a non-classical phenotype, while the proportion of underweight patients is relatively high, especially in women.
- Although the average BMI was within the normal range before and after the GFD, it increased significantly even at short-term follow-up.
- The significant difference in BMI between the classical and non-classical cases at diagnosis disappears in the short term,but becomes significant again in the long term as the BMI values of the non-classical group increase.
- The number of overweight people on a GFD increases in the long term, especially in men and non-classical clinical presentations.
- CV and metabolic consequences in the management of obesity-related issues are a new challenge in the care of patients with CD.

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7. Scientometrics

Scientific papers

- Total: 22
- English-language: 16

Impact factor

- As first author: 14.4
- Cumulative: 30.7

Citations

- Independent: 50
- Cumulative: 55
- Hirsch index: 3

List of publications

Papers upon which this thesis relies (n=2, cumulative impact factor: 9.6)

1. **Vereczkei Z**, Dergez T, Fodor Z, Szakács Z, Bajor J. Body Mass Index during Gluten-Free Diet in Patients with Celiac Disease. *Nutrients*. 2023;15(16):3517. doi:10.3390/nu15163517 **(IF: 4.8, D1)**
2. **Vereczkei Z**, Farkas N, Hegyi P, et al. It Is High Time for Personalized Dietary Counseling in Celiac Disease: A Systematic Review and Meta-Analysis on Body Composition. *Nutrients*. 2021;13(9):2947. doi:10.3390/nu13092947 **(IF: 4.8, D1)**

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1. **Vereczkei Z**, Szakács Z, Peresztegi MZ, et al. Influence of a structured, 1-year-long dietary intervention regarding body composition and cardiovascular risk (ARCTIC) in coeliac disease: a protocol of a multicentre randomised controlled trial. *BMJ Open*. 2024;14(10):e084365. doi:10.1136/bmjopen-2024-084365 **(IF: 2.4, Q1)**
2. **Vereczkei Z,** Fülöp P, Lada S, et al. Coeliakiás betegek mediterrán diéta adherenciája. Prospektív, multicentrikus vizsgálat (ARCTIC study) eredményei. *Central European Journal of Gastroenterology and Hepatology/ Gasztroenterológiai és Hepatológiai Szemle.* 2024;10(S1):138.
3. Lemes K, Lénárt Z, Lada S, … **Vereczkei Z,** …et al. Újonnan diagnosztizált cöliákiás betegek testösszetétel paramétereinek vizsgálata prospektív, multicentrikus, eset-kontroll vizsgálat (ARCTIC study) előzetes eredményei. *Central European Journal of Gastroenterology and Hepatology/ Gasztroenterológiai és Hepatológiai Szemle.* 2024;10(S1):109-110.
4. Peresztegi M, **Vereczkei Z,** Sipos Z, et al. Investigation of body composition parameters in patients with celiac disease on a gluten-free diet. Prospective, multicenter, case-control study (ARCTIC study). *Central European Journal of Gastroenterology and Hepatology/ Gasztroenterológiai és Hepatológiai Szemle*. 2024;10(S1):122-123.

5. Bajor J, Peresztegi M, **Vereczkei Z,** et al. Hepatic steatosis in celiac disease. Results of a prospective, multicenter, case-control study (ARCTIC study). *Central European Journal of Gastroenterology and Hepatology/ Gasztroenterológiai és Hepatológiai Szemle.* 2024;10(S1):74-75.
6. Bajor J, Peresztegi M, **Vereczkei Z, et al.** Investigation of gluten immunogenic peptide in celiac disease. *Central European Journal of Gastroenterology and Hepatology/ Gasztroenterológiai és Hepatológiai Szemle.* 2024;10(S1):74.
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8. **Vereczkei Z,** Fülöp P, Lada S, et al. Body composition and mediterranean diet adherence of coeliac patients. A prospective, multicenter study (ARCTIC study). *United European Gastroenterology Journal.* 2024;12(S8):828.
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11. Szakács Z, Farkas N, Nagy E, Bencs R, **Vereczkei Z**, Bajor J. Clinical Presentation Is Dependent on Age and Calendar Year of Diagnosis in Celiac Disease: A Hungarian Cross-Sectional Study. *Journal of Personalized Medicine*. 2023;13(3):487. doi:10.3390/jpm13030487 **(IF: 3.0: Q2)**
12. **Vereczkei Z**, Imrei M, Szakács Z, et al. Cardiovascular risk factors in coeliac disease (ARCTIC): a protocol of multicentre series of studies. *BMJ Open*. 2023;13(9):e068989. doi:10.1136/bmjopen-2022-068989 **(IF: 2.4, Q1)**
13. Peresztegi M, **Vereczkei Z**, Farkas N, Szakács Z, Bajor J. A coeliakia változó klinikai megjelenését befolyásoló tényezők. *Magyar Belorvosi Archivum.* 2023;76(5-6):329.
14. **Vereczkei Z,** Farkas N, Hegyi P, et al. Changes in body composition among patients with coeliac disease: a systematic review and meta-analysis. *United European Gastroenterology Journal.* 2021;9(8):344.

Other papers not related to the topic of the thesis (n=6)

1. Nagy R, Gede N, Ocskay K, … **Vereczkei Z**, …et al. Association of Body Mass Index With Clinical Outcomes in Patients With Cystic Fibrosis: A Systematic Review and Meta-analysis. *JAMA Network Open*. 2022;5(3):e220740. doi:10.1001/jamanetworkopen.2022.0740 **(IF: 10.5, D1)**

2. Juhász MF, **Vereczkei Z**, Ocskay K, et al. The EFFect of dietary fat content on the recurrence of pancreaTitis (EFFORT): Protocol of a multicenter randomized controlled trial. *Pancreatology*. 2022;22(1):51-57. doi:10.1016/j.pan.2021.10.002 **(IF: 2.8, Q1)**
3. Fekete K, Merkl Z, Pákai E, … **Vereczkei Z**, …et al. Az újszülöttkori kihűlés jelentősége és kísérletes modellezése. Egészség-Akadémia. 2022;13(3-4):113-118.
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5. **Vereczkei Z**, Szekeresné Szabó S, Pótó L, Vereczkei A. A korai posztoperatív enterális táplálás megvalósulásának gyakorlata colorectalis daganatos betegeknél. *Táplálkozástudományi és Dietetikai Szemle*. 2021;1(1):27-34.
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List of conference abstracts

List of conference presentations/posters related to the topic of the thesis (n=13)

1. Peresztegi M, **Vereczkei Z**, Farkas N, et al. Investigation of body composition parameters in patients with celiac disease on a gluten-free diet. Prospective, multicenter, case-control study (ARCTIC study). United European Gastroenterology Week (UEGW), Bécs, 2024. október 12-15.
2. Bajor J, Peresztegi M, **Vereczkei Z**, et al. Hepatic steatosis and body composition in patients with celiac disease. Preliminary results of a prospective, multicenter, case-control study (ARCTIC study). United European Gastroenterology Week (UEGW), Bécs, 2024. október 12-15.
3. **Vereczkei Z**, Fülöp P, Lada S, et al. Body composition and Mediterranean diet adherence of coeliac patients. A prospective, multicenter study (ARCTIC study). United European Gastroenterology Week (UEGW), Bécs, 2024. október 12-15.
4. Peresztegi M, **Vereczkei Z**, Máth B, et al. Cardiovascular risk factors in celiac patients. Results of a prospective, multicenter, case-control study (ARCTIC study). Hungarian Medical Association of America (HMAA) konferencia, Várgesztes, 2024. szeptember 6-7.
5. **Vereczkei Z**, Fülöp P, Lada S, et al. Evaluation of body composition and Mediterranean diet adherence in coeliac patients. Preliminary results of the ARCTIC study. World Digestive Health Congress, Barcelona, 2024. augusztus 29-31.
6. Lemes K, Lénárt Z, Lada S, …**Vereczkei Z**, …et al. Újonnan diagnosztizált cöliákiás betegek testösszetétel paramétereinek vizsgálata prospektív, multicentrikus, eset-kontroll vizsgálat (ARCTIC study) előzetes eredményei. Magyar Gasztroenterológiai Társaság 66. Nagygyűlése, Siófok, 2024. május 30-június 2.

7. Bajor J, Peresztegi M, **Vereczkei Z**, et al. Hepatic steatosis in celiac disease. Results of a prospective, multicenter, case-control study (ARCTIC study). Magyar Gasztroenterológiai Társaság 66. Nagygyűlése, Siófok, 2024. május 30-június 2.
8. Bajor J, Peresztegi M, **Vereczkei Z,** et al. Investigation of gluten immunogenic peptide in celiac disease. Magyar Gasztroenterológiai Társaság 66. Nagygyűlése, Siófok, 2024. május 30-június 2.
9. Peresztegi M, **Vereczkei Z**, Sipos Z, et al. Investigation of body composition parameters in patients with celiac disease on a gluten-free diet. Prospective, multicenter, case-control study (ARCTIC study). Magyar Gasztroenterológiai Társaság 66. Nagygyűlése, Siófok, 2024. május 30-június 2.
10. **Vereczkei Z**, Fülöp P, Lada S, et al. Coeliakiás betegek mediterrán diéta adherenciája. Prospektív, multicentrikus vizsgálat (ARCTIC study) eredményei. Magyar Gasztroenterológiai Társaság 66. Nagygyűlése, Siófok, 2024. május 30-június 2.
11. Peresztegi M, **Vereczkei Z**, Farkas N, Bajor, J. Investigation of cardiovascular risk factors, metabolic parameters, and body composition in celiac patients. International Conference for Healthcare and Medical Students (ICHAMS), Dublin, 2024. február 15-17.
12. Peresztegi M, **Vereczkei Z**, Farkas N, Szakács, Z, Bajor, J. A coeliakia változó klinikai megjelenését befolyásoló tényezők. Magyar Belgyógyász Társaság 49. Nagygyűlése, Visegrád, 2023. november 16-18.
13. **Vereczkei Z**, Farkas N, Hegyi P, et al. Changes in body composition among patients with coeliac disease: a systematic review and meta-analysis. United European Gastroenterology Week (UEGW), online, 2021. október 3-5.