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ORIGINAL ARTICLE

A comparison of the nutritional status between adult celiac patients on a long-term, strictly gluten-free diet and healthy subjects

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BACKGROUND/OBJECTIVES: There are conflicting data on the effect of a gluten-free diet (GFD) on the nutritional status of celiac patients. In the present study, we evaluated, in adult celiac patients, the influence of a long-term, strictly GFD on their nutritional status and compared it with matched healthy volunteers.

SUBJECTS/METHODS: Our study included 39 celiac patients and 39 healthy volunteers. The body mass index (BMI) of patients and controls was evaluated at enrollment, while the patients' BMI before the GFD was retrieved from clinical records. In addition, at enrollment, in both groups, we compared BMI, fat mass (FM), bone mineral density (BMD), as well as their dietary intake, recorded on a 7-day diary.

RESULTS: At the time of diagnosis, the majority of celiac patients (82.0%) had a normal BMI or were overweight, while 10.3% were malnourished. After the GFD, patients with a normal BMI showed a significant weight increase ($P = 0.002$), but none of them switched in the overweight or obese category. Two (50%) of the four malnourished patients achieved a normal BMI. Controls and patients on a GFD had a similar BMI, FM, BMD and total calorie intake, but the amount of lipids and fiber intake was significantly different in the two groups ($P = 0.003$ and $P < 0.0001$, respectively).

CONCLUSIONS: Our study demonstrates that a GFD is able to improve the nutritional status of celiac patients without inducing overweight or obesity. Our findings are related to a celiac population adopting a GFD based on a Mediterranean-type diet.

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INTRODUCTION

Celiac disease (CD) is an autoimmune enteropathy caused by a permanent intolerance to gluten in genetically susceptible individuals.[1] Actually, CD represents one of the most common autoimmune-based disorder affecting about 1% of Western population, while a decade ago it was considered a rare disease outside Europe and, therefore, underestimated by healthcare professionals.[2–4]

CD shows different clinical presentations: symptomatic cases show intestinal (chronic diarrhea, weight loss) or extraintestinal (anemia, osteoporosis, neurological disturbances) features; silent forms are occasionally discovered because of serological screening; potential forms present autoantibodies but no evident autoimmune-induced injury of the intestinal mucosa.[5–8]

Newly diagnosed celiac patients or those not complying with a gluten-free diet (GFD) are demonstrated to have an imbalance of macronutrients, low fiber intake and micronutrient deficiency.[9] In addition, about 40–70% of celiac patients have low bone mineral density (BMD), osteoporosis, osteomalacia and secondary hyperparathyroidism.[9,10] Nevertheless, the majority of celiac patients have a normal or elevated body mass index (BMI) at diagnosis.[11–13]

A GFD is the only current treatment for patients with CD and is associated with a marked improvement/restoration of the intestinal mucosa integrity, disappearance of the symptoms and normalization of laboratory findings.[14]

Although various studies conducted over 10 years ago, two Italian and one Danish, revealed a state of mild malnutrition (low BMI, low fat mass (FM) and low BMD) in celiac patients despite a GFD,[10,14,15] two more recent studies conducted in a large population of Irish and North American patients highlighted the development of overweight and obesity among patients.[11,16] However, another recent North American study, conducted in a large celiac population, attributes beneficial effects of a GFD on the BMI, demonstrating a switch to a lower BMI category of 16.7% of overweight and 5.9% of obese patients, and a switch to a higher BMI category in 47.5% of underweight patients.[13]

To the best of our knowledge, this is the first study of CD patients to focus simultaneously on the following aspects: (1) evaluation of the BMI before and after a GFD, (2) body composition and BMD with the GFD, (3) quantitative and qualitative (macronutrients, fibers and cholesterol) aspects of the diet and (4) comparison of all these parameters between

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patients under GFD and healthy controls, matched for sex, age and social status.

Our intent was to evaluate, in adult celiac patients, the influence of a long-term, strictly GFD on their nutritional status and compared it with matched healthy volunteers. To achieve this goal, the patients' BMI recorded before the GFD was compared with the BMI evaluated after a median period of 2 years of strict compliance with a GFD. In addition, at enrollment, the BMI, FM, BMD and dietary intake in CD patients was compared with that of healthy matched volunteers.

MATERIALS AND METHODS

Study design

In the present study, we included 39 patients who had been on a strict GFD for a median time of 24.3 months (20.2–35.6 months). They were attending as outpatients at our Gastroenterology Unit and had a previous serology- and histology-proven diagnosis of CD.

The study protocol was conducted in accordance with the Declaration of Helsinki Principles and written informed consent was obtained, before enrollment, from all participants in the study. The study was approved by the local Ethics Committee.

As reported in the medical records, the diagnosis of CD was based on positive anti-transglutaminase/anti-endomysium antibodies and histological evaluation of the duodenal mucosa. On the basis of the Marsh–Oberhuber classification,[17] all patients showed increased intraepithelial lymphocytes, hypertrophic crypts and mild to marked villous atrophy (type 2–3b); no patient had a completely flat mucosa (type 3c). The data reported on anti-transglutaminase immunoglobulin A, assessed every 6–12 months, checked compliance to the GFD, as suggested by Italian guidelines.[18] Patients positive to anti-transglutaminase antibodies or with endocrine disorders, hepatic or renal disease, pregnant or taking drugs that could influence the nutritional status (corticosteroids and thyroid hormones), were excluded from the study.

At enrollment, that was done about 2 years after starting the GFD, patients were invited to attend the study together with a relative or a friend, who was enrolled as a healthy volunteer if shown to have negative anti-transglutaminase antibodies (control). Thirty-nine controls were matched for sex, age and social status (evaluated on the basis of educational attainment, current income and lifetime occupation).[19] It is important to note that controls were free to continue on their normal diet. At enrollment, the patients' BMI was calculated and compared with their BMI at the time of diagnosis, retrieved from their medical records. In addition, at enrollment, the BMI, FM, BMD and dietary intake were compared in CD patients and healthy matched volunteers.

Body mass index

Body weight (Kg) and height (m) were measured barefoot. The BMI was calculated as weight divided by squared height (kg/m^2). According to the World Health Organization classification, patients were considered malnourished with a BMI < 18.5, normal weight in the BMI range from 18.5 to 24.9, overweight with a BMI between 25 and 30 and obese with a BMI > 30.[20]

Body-composition analysis and BMD

Analysis of the body composition and BMD was performed by dual-energy X-ray absorptiometry.[21,22] Dual-energy X-ray absorptiometry was performed with a Hologic QDR 2000 device (Waltham, MA, USA) to determine the FM (expressed as percentage of body weight) and BMD.

Measurements were made at the lumbar spine (L2–L4) and hip, and at the whole skeleton. BMD was expressed as grams of hydroxyapatite/cm^2. Great care was taken in positioning the subjects and identifying the zones for analysis, which are the main sources of error. The precision of our Hologic device was 1.2% for the lumbar spine, 1.6% for the femoral neck, 1.8% for the trochanter and 3% for the Ward's triangle. Throughout the study, the long-term stability of the instrument was monitored on a daily basis, checking the accuracy and reproducibility obtained by using an object with a constant mass. The coefficients of variation of the Hologic Densitometers were between 0.30% and 0.45% for BMD per year. All scans were reviewed by a blinded expert and reanalyzed when necessary. Osteoporosis was defined as a low BMD, at least 2.5 s.d. below the mean of young normal individuals (*T*-score), or below the mean of age-matched controls (*Z*-score) for the hip and the lumbar spine (L2–L4). Osteopenia was defined as a BMD of > 1.0 but < 2.5 s.d. below the mean of young normal individuals (*T*-score), or of age-matched controls (*Z*-score).[21,22]

Dietary evaluations

Each participant in the study was asked to fill out a 7-day food diary at enrollment. A dietician instructed patients and controls on how to fill out a detailed daily report on the food and beverages consumed. If the diary resulted incomplete or incorrect, participants were asked to repeat the report for another week. A computerized program (Winfood 2.7 Medimatica Srl, Colonnella, Italy) was employed to evaluate food energy content and qualitative aspects of the diet (macronutrients, fibers and cholesterol). The composition of gluten-free food was determined according to the manufacturers' information reported on packages.

Statistical analysis

Our results were expressed as number (percentage) or median (with interquartile range) or means ± s.d.

Comparisons were made by χ^2-test for dichotomous variables, and Wilcoxon rank test and Kruskal–Wallis test for paired and unpaired continuous variables, respectively. A two-sided *P*-value < 0.05 was considered statistically significant in the case-control analysis. All analyses were performed using R Statistical Software (Foundation for Statistical Computing, Vienna, Austria).

RESULTS

At enrollment, celiac patients and controls were matched for sex (Male:Female 9/30 vs 11/28, $P = 0.5$ by χ^2-test), age (35 years (25–45) vs 33 years (21–45), $P = 0.8$ by Kruskal–Wallis test) or BMI (22.6 (21.1–25.2) vs 22.2 (20.7–26.0), $P = 0.39$ by Kruskal–Wallis test). Only a trend toward increase was observed when the BMI values of all patients were compared before and after complying with the GFD (Table 1). However, when we considered the distribution of celiac patients in the four BMI categories (malnourished, normal, overweight and obese) and compared the BMI of the same patients before and after GFD, we found that there was a

Table 1. BMI value in celiac patients before and after GFD

	No. of patients before GFD	*No. of patients after GFD*	*BMI before GFD*	*BMI after GFD*	P-*value*[a]
Total	39 (100%)	39 (100%)	21.5 (20.4–25.1)	22.6 (21.1–25.2)	0.07
Obese	3 (7.7%)	3 (7.6%)	38.0 (36.2–39.4)	35.0 (33.1–36.7)	0.31[b]
Overweight	9 (23.0%)	8 (20.5%)	25.2 (25.2–26.0)	25.2 (24.5–26.0)	0.47[b]
Normal	23 (59.0%)	26 (66.6%)	20.7 (20.4–21.7)	22.5 (21.1–23.1)	0.002[b]
Malnourished	4 (10.3%)	2 (5.1%)	18.0 (17.6–18.0)	18.0 (17.7–18.2)	0.41[b]

Abbreviations: BMI, body mass index; GFD, gluten-free diet; IQR, interquartile range. [a]Differences between BMI values were assessed by Wilcoxon rank test. [b]*P*-values were calculated comparing the same patients before and after GFD. BMI is expressed as median (IQR).

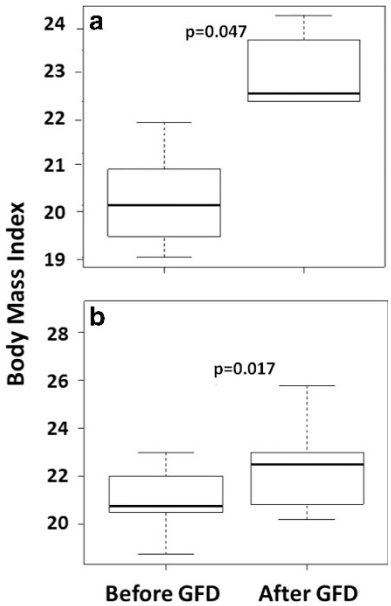

Figure 1. BMI in male and female celiac patients with normal BMI, before and after GFD. Values were expressed as median (IQR). (**a**) Male, *$P = 0.047$ by Wilcoxon rank test. (**b**) Female, **$P = 0.017$ by Wilcoxon rank test.

statistically significant increase of the BMI ($P = 0.002$) in the normal BMI category, which included the majority of patients (Table 1).

As shown in Figure 1, when the latter category of patients was stratified by gender, the BMI still remained significantly increased after GFD, in both the five males and the 18 females ($P = 0.047$ and $P = 0.017$, respectively).

In addition, all obese patients remained obese after GFD and only one patient (11%) in the overweight category dropped into the normal BMI category (Table 1). As far as the four malnourished patients were concerned, two (50%) remained in the same category and two (50%) achieved a normal BMI (Table 1).

A comparison of the BMI in celiac patients after dietary treatment versus controls is reported in Table 2. Interestingly, our analysis demonstrates that the BMI was similar in the two groups. The evaluation of FM and BMD by dual-energy X-ray absorptiometry, performed in all CD patients ($n = 39$) and in 28 of 39 controls ($n = 22$ females, $n = 6$ males, $P = 1.0$; median age: 36 years (24–43), $P = 0.9$), demonstrated a similar FM in cases and controls after stratifying subjects by gender (Table 2). Finally, the BMD and *T*-score did not differ between patients and controls (Table 2).

As shown in Table 3, the 7-day food diary filled out by patients and controls did not demonstrate significant differences in calorie ($P = 0.21$), protein ($P = 0.14$) and carbohydrate intake ($P = 0.8$). However, celiac patients on a GFD had a significantly higher lipid intake ($P = 0.003$), but not higher cholesterol ($P < 0.37$), and had a lower intake of fiber as compared with controls ($P = 0.0001$). In CD patients and controls, calcium, vitamin D and phosphorus intake were in the normal range (data not shown) of the Italian recommended daily allowance.[23]

DISCUSSION

Our study shows that, in agreement with recent data in the literature, the majority of celiac patients (82%) had a BMI in the normal or overweight range and only 10% were malnourished at the time of diagnosis.[11–13,16]

Table 2. BMI and DEXA values simultaneously assessed in celiac patients after GFD and controls

	Celiac patients	*Controls*	P-*value*[a]
FM in men (%)	19.4 ± 5.6	20.3 ± 5.6	0.76
FM in women (%)	33.1 ± 5.3	32.4 ± 6.2	0.66
BMD (g/cm^2)	0.99 ± 0.14	0.98 ± 0.15	0.77
T-score	-0.53 ± 1.12	-0.69 ± 1.34	0.58

Abbreviations: BMI, body mass index; CD, celiac disease; DEXA, dual-energy X-ray absorptiometry: FM, fat mass; GFD, gluten-free diet. [a]Statistical analysis for unpaired continuous variables was performed by Kruskal–Wallis test. Data reported were expressed as means ± s.d. to allow a comparison with the data of the literature. FM and BMD were performed in 39 CD patients and 28 controls. *T*-score in general population: value $\geqslant -1$ (normal), value < -1 and $\geqslant -2.5$ (osteopenia) and value < -2.5 (osteoporosis).

Table 3. Total caloric daily intake and food composition in celiac patients and controls

	Celiac patients GFD	*Controls*	P-*value*
Kcal/day	1693.9 ± 581.9	1551.5 ± 362.1	0.21
Protein (g/day)	65.9 ± 20.7	59.3 ± 16.8	0.14
Carbohydrate (g/day)	207.9 ± 95.5	212.5 ± 58.1	0.80
Lipid (g/day)	67.2 ± 20.1	55.0 ± 13.5	0.003[a]
Cholesterol (g/day)	187.8 ± 69.1	172.3 ± 72.9	0.37
Total Fiber (g/day)	7.3 ± 4.9	12.8 ± 4.4	< 0.0001[a]

Abbreviation: GFD, gluten-free diet. [a]Statistical analysis was performed by Kruskal-Wallis test. Data reported, obtained from all patients and controls, were expressed as means ± s.d. to allow a comparison with the data of the literature.

After the treatment with a GFD, there was a general trend toward an increased BMI. This increase reached statistical significance in patients of both sexes with a normal BMI, and none of the celiac patients moved into the overweight or obese category. Finally, 50% of our malnourished patients (two out of four) achieved a normal BMI, as reported in other studies.[11,13,16] Presumably, this was a positive consequence of the GFD. On the other hand, the reason why the other two patients did not have an improved BMI is more difficult to explain. This phenomenon, also reported by others, has been justified by poor compliance with the GFD.[16] In our opinion, it is unlikely that those patients who would derive the greatest benefit from compliance with a GFD, that is, malnourished patients, would be the only ones who did not strictly adhere to the GFD. In addition, our selection criteria guaranteed an optimal compliance of patients to the GFD since the routinely prescribed laboratory tests in the celiac outpatients included an anti-transglutaminase antibody test, that can discriminate between patients who were strictly or only partially compliant to the diet.[24]

Another important aspect highlighted by our findings is that after a GFD, celiac patients had similar BMI values to those observed in healthy subjects matched for sex, age and social status. In addition, the FM values in CD patients who had been on a GFD for 24 months were similar to those in matched controls (Table 3) and in the Italian population belonging to the same sex and age groups.[25]

Celiac patients on a strict GFD had a *T*-score and a BMD comparable to controls, as reported in Table 2. The *T*-score is the parameter used to define the condition of normality, osteopenia and osteoporosis, as it takes in account multiple aspects such as

BMD, age and sex. In our study, CD patients had a *T*-score that ranged between normality and osteopenia. These findings are in apparent contradiction to the data reported by Kurppa *et al.*[26] in CD patients, describing no improvement of BMD after a 1-year GFD. This was probably due to the fact that we assessed BMD after 2 years, which are sufficient to increase the bone mass, as reported by Passananti *et al*.[27]

More than 10 years ago, CD was diagnosed in most patients only when they became symptomatic. Moreover, they were more easily, inadvertently, exposed to gluten (due to the lack of information and the lesser availability of specially manufactured and labeled gluten-free food). This could justify the difference between our results and those reported by previous studies, showing a state of mild malnutrition despite of compliance to a GFD as compared with control subjects.[10,14,15] On the other hand, our findings do not show an alarming incidence of obesity among celiac patients on GFD, as reported by more recent studies.[11,16] This is probably due to the low daily calorie intake of our patients and controls, that was clearly lower than the recommended daily allowance of nutrients for the Italian population.[23] Moreover, in a large case-control study, Cheng *et al.*[13] show an overall body weight reduction in overweight and obese celiac patients supporting our findings. Finally, our CD patients were on a Mediterranean-type diet that is different from the high-fat/high-sugar 'Western' diet, which is able to alter the composition and metabolic activity of our gut microbiome.[28] Such diet-induced changes are now suspected to contribute to obesity.[29,30]

In agreement with the data from the literature,[31] we found a significantly higher intake of lipids in celiac patients as compared with controls ($P = 0.003$), but no significant difference as far as cholesterol intake was concerned. This was not surprising as it is known that gluten-free bakery products contain a higher amount of lipids than the equivalent gluten-containing food.[32] Although some authors have reported a reduced carbohydrate intake in celiac patients on a GFD,[31] we did not find any significant difference in the consumption of carbohydrates and protein and the total calorie intake when comparing the dietary intake in CD patients with that in controls. This result could be related to the large consumption of baked food, pasta, bread and pizza in South Italy, where our celiac population lives. Finally, as reported by other authors,[9] we demonstrated a statistically significant lower fiber intake in celiac patients as compared with controls ($P < 0.0001$). This was probably due to the lower content of fiber in the GFD products as reported by others.[9]

Our study presents some limitations such as the small number of subjects enrolled and the low number of underweight patients, that are insufficient to represent the general population. However, other studies on CD patients aiming to assess body composition and BMD[10,15,26] were also conducted in a limited number of patients due to the difficulty of evaluating these parameters on a large scale. Moreover, our selection criteria, by taking into account, age, sex and social status, guaranteed a good match of the population samples. Finally, the percentages of patients in the four BMI categories reflect the data reported in larger studies.[11,16] The assessment of body composition and BMD of patients at diagnosis, would have helped us to better interpret our results after 2 years of a GFD. However, it is not likely that our patients had a normal BMD at diagnosis as a low BMD is a condition commonly observed in the CD.[9,10] As far as the body composition, our goal was to exclude the development of a condition of overweight or obesity and not to evaluate possible changes regarding FM and fat free mass after a GFD.

In conclusion, our study demonstrates that a GFD is able to improve the nutritional status of celiac patients complying with a Mediterranean style diet, without causing them to become overweight or obese, as has previously been described in celiac patients on a Western diet. Our patients showed a similar BMI, body composition and BMD to those in normal subjects. The effect of long-term consumption of a high-lipid/low-fiber diet on the BMI and general health status of CD patients is an aspect that has to be fully explored still.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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