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Original article

Dietary intake of patients with inflammatory bowel disease: A comparison with individuals from a general population and associations with relapse

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SUMMARY

Background and aims: Individuals with inflammatory bowel disease (IBD) often hold strong beliefs on how diet impacts their disease. This study aimed to compare dietary intakes between IBD patients and individuals from the general population and to assess associations of dietary factors with relapse in patients with IBD.

Methods: Patients with longstanding Crohn's disease and ulcerative colitis (n = 165) filled out food frequency questionnaires, as did individuals participating in a Dutch population-based study (controls) (n = 1469). Multivariable regression analyses were used to assess differences in habitual dietary intake between IBD patients and controls, and to estimate associations of dietary factors in patients in remission with the development of disease relapse at follow-up.

Results: IBD patients had higher intakes of animal protein (3.50 g/d, 95% confidence interval (CI) 1.67 −5.34) and carbohydrate (10.1 g/d, 95% CI 5.23−14.9) than controls and lower intakes of (unsaturated) fat (−3.53 g/d, 95% CI −5.57− −1.50), dietary fiber (−2.19 g/d, 95% CI −3.05− −1.32) and alcohol (−0.84 g/d, 95% CI −1.46− −0.22). This was explained by a higher consumption of carbonated beverages, meat and poultry and lower consumption of fruit, vegetables and dairy products (except cheese) by IBD patients compared with controls. Several dietary factors, particularly (saturated) fat and fiber, appeared to be associated with risk of relapse.

Conclusions: IBD patients had higher dietary intakes of (animal) protein and carbohydrate and lower intakes of (unsaturated) fat, dietary fiber and alcohol compared with a general Dutch population. The results further underscore that dietary factors may have a role in disease course.

Introduction

Crohn's disease (CD) and ulcerative colitis (UC) are believed to result from an interaction between genetic and environmental influences, but the pathogenesis of these chronic, relapsing inflammatory bowel diseases (IBDs) is not fully understood. Diet is likely to play an important role through different biological mechanisms, including the presentation of dietary antigens and modification of the gut microbiota [1]. However, robust evidence to support the concept that patients with IBD might benefit from dietary modification is lacking [2,3].

Even so, patients with IBD often strongly belief that diet plays a key role in controlling their disease [4–7]. Studies on dietary behavior indicate that more than half of CD and UC patients believe that food can be a trigger for disease relapse [6,7]. Accordingly, the majority of patients report that they avoid certain foods, such as spicy or fatty food, in order to prevent a relapse [6,7]. Assessments

Abbreviations: CD, Crohn's disease; CI, confidence interval; IBD, inflammatory bowel disease; IQR, interquartile range; NQplus, Nutrition Questionnaires plus (study); OR, odds ratio; UC, ulcerative colitis.

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of dietary intakes of IBD patients with longstanding disease or actual comparisons with the general population are, however, limited [5,8,9].

Although associations between preillness diet and the risk of developing CD and UC have frequently been explored [10], only few studies have evaluated the putative impact of habitual diet on the clinical course of patients with established IBD [11,12]. In a prospective cohort study, consumption of meat, protein and alcohol was found to be associated with an increased risk of relapse in UC patients, which was thought to be associated with intake of sulfur and sulfate [13]. For CD, fat intake has been linked with active disease [14], although reports are conflicting [15]. Consumption of dietary fiber has been associated with a reduced risk of developing flares in CD [16].

The aims of this study were to compare dietary intakes between IBD patients and individuals from the general population and to determine associations of dietary factors with relapse in patients with IBD at follow-up.

Methods

Study population and data collection

This study included a cross-sectional part comparing dietary data obtained from IBD patients and unaffected individuals from a general Dutch population (controls). In addition, the association of dietary intake with the clinical course of disease among IBD patients was explored longitudinally by evaluating the development of relapse after assessment of their habitual diet.

Patients aged 18–70 years with CD, UC or IBD-unclassified were enrolled in a colorectal cancer surveillance program at the University Medical Center Utrecht in the Netherlands. Individuals with a history of (sub)total colectomy were excluded. Patients underwent regular colonoscopic surveillance, during which disease activity was assessed. The medical records of subjects were reviewed and patients were asked to fill out a questionnaire regarding medication use, education, anthropometric measures and smoking. Patients also completed a food frequency questionnaire (FFQ). Endoscopic data were used to determine disease activity at the time of completion of the questionnaire. Medical records were used in patients who completed the questionnaire more than eight weeks before or after endoscopic surveillance. In these cases, disease remission was defined as stable treatment without clinical or biochemical signs of active disease observed at outpatient clinic visits.

Individuals participating in the Nutrition Questionnaires plus (NQplus) study served as controls from the background population (comparison group). This observational study was initiated to examine diet and health in individuals from the general Dutch population. Participants aged 20–77 years were recruited between 2011 and 2013 by inviting randomly selected inhabitants (n = 70,000) from several towns located in the central part of the Netherlands [17,18]. Participants registered online. A total of 2048 individuals agreed to participate in the NQplus study [19]. Data on demographics, history of disease, education and lifestyle, including physical activity and smoking, were self-reported. A total of 1657 participants also completed a FFQ. The proportion of men and women and married individuals of participants of the NQplus study was similar to that of the general Dutch population [20]. The proportion of smokers among participants of the NQplus study appears to be lower than among the general Dutch population, whereas NQplus participants received a higher level of education. Intake of macronutrients of participants of the NQplus study was representative for the general Dutch population when compared to the Dutch National Food Consumption Survey [21].

Dietary assessment

A self-completed, semiquantitative FFQ was used to assess individuals' habitual dietary intake. The FFQ used in IBD patients was an adapted version of the FFQ applied in the NQplus study. In the adapted version, the following food items were broken down into additional questions: meat (questions about intake of red, white and processed meat), dairy products (questions about intake of fermented and nonfermented dairy products) and vegetables (questions about intake of leafy, yellow and cruciferous vegetables). Questions concerning all other food items and also the format of questions and answer categories were entirely the same for the FFQs. The FFQs were validated previously [22,23]. The FFQs captured the intake of foods consumed during the previous month and were designed for the Dutch population. The Dutch Food Composition Table was used to calculate daily energy and nutrient intake [24]. Food items were also categorized into different food groups according to this database: coffee/tea, carbonated beverages, fruits and vegetables, grains, dairy products (milk products and cheese), sugar and sweets, fats/oils/savory sauce and meats, poultry and fish. These food groups were selected based on two recent studies on dietary beliefs and practices in which these foods were reported to be frequently avoided by IBD patients to prevent a relapse of their disease [6,7].

The ratio of energy intake to estimated basal metabolic rate was calculated for each individual to evaluate underreporting and overreporting [25,26]. The following items were assumed based on previous reports: within-subject variation in energy intake of 23%, within-subject variation in estimated basal metabolic rate of 8.5%, a physical activity level of 1.55 and a between-subject variation in physical activity level of 15% [22,26]. Participants with a ratio lower than 0.87 or higher than 2.75 were considered as underreporters or overreporters, respectively, and removed from the analyses [26]. Among female participants of the NQplus study, the proportion of underreporters and overreporters was 10.1% (n = 80) and 0.3% (n = 2), respectively, whereas 20.0% (n = 24) of female IBD patients were underreporters and 0.8% (n = 1) were overreporters. The proportion of underreporters was 11.8% (n = 102) among male participants of the NQplus study and 12.4% (n = 11) among male IBD patients. The proportion of overreporters was 0.2% (n = 2) among male participants of the NQplus study and 1.1% (n = 1) among male IBD patients. Thirty-seven participants of the NQplus study deliberately followed a energy-restricted diet and were therefore included, whereas participants with a self-reported diagnosis of CD or UC or those with missing data on history of IBD (n = 39) were excluded. This resulted in 165 IBD patients and 1469 individuals from the NQplus study for the definitive analyses.

Follow-up

In IBD patients in remission at the time of FFQ completion, the clinical disease course following FFQ administration was assessed by evaluation of medical records. Relapse was defined as (1) a step-up in IBD medication, (2) endoscopy showing active disease, (3) hospitalization due to active IBD or (4) surgery related to IBD. Patients were followed from the date of FFQ administration until relapse or end of follow-up.

Statistical analysis

Categorical outcomes were expressed as frequencies with proportions and were compared using the chi-squared test. Continuous outcomes were presented as medians with interquartile ranges (IQRs) or as means with standard deviations (SDs) and were compared with the Mann–Whitney U test or the Student's t-test, as

appropriate. Multivariable linear regression was performed to determine differences in dietary intakes between IBD patients and controls using dietary outcome as the dependent variable and patient/control status as the independent variable. Regression coefficients (betas) with 95% confidence intervals (CIs) were estimated. These coefficients indicate mean differences in dietary intakes between the two groups and were adjusted for age (continuous variable), body mass index (continuous variable), smoking status (categorized into never smoker, former smoker and current smoker using dummy variables), plus gender and energy intake (continuous variable). Skewed dietary outcomes were $\log_2$-transformed. In this case, a beta of 1, for example, corresponds with a twofold (2^1) higher intake of the dietary variable in IBD patients compared with controls. Intakes of energy, nutrients and foods were expressed as medians with IQRs. Among IBD patients in remission, multivariable logistic regression was performed to assess associations between dietary factors and risk of relapse at follow-up using relapse (categorized into yes or no) as the dependent variable and dietary intakes as the independent variable. Odds ratios (ORs) with 95% CIs were obtained. Dietary intakes were introduced in models as high/low intake based on the median level among patients ('categorical analysis') and as a continuous variable ('continuous analysis'). Logistic regression analyses were adjusted for gender, age (continuous variable) and energy intake (continuous variable). In a further analysis, additional adjustment for body mass index (continuous variable), smoking status (categorized into never smoker, former smoker and current smoker) and use of steroids or biologicals (both categorized into yes or no) was performed. A two-sided p-value below 0.05 was considered to indicate statistical significance. Statistical analyses were performed using SPSS version 21 (IBM Corp, Armonk, New York, United States).

Ethical considerations

Approval was obtained from the relevant institutional ethics committees and all individuals provided written informed consent.

Results

Characteristics of patients and controls

In total, 165 patients with IBD and 1469 individuals from the general population participating in the NQplus study were included. The general characteristics of patients and controls are shown in Table 1. Differences in age, body mass index and smoking status between the two groups were observed. The disease characteristics of patients at baseline are listed in Supplementary Table 1. Of the 165 IBD patients, 91 (55%) had CD and 68 (41%) had UC. The remaining 6 patients (4%) had IBD-unclassified. The median disease duration was 19 years. Of the patients with CD, 46 (51%) had colonic disease and 45 (49%) had ileocolonic disease. Regarding UC and IBD-unclassified, 42 (57%) patients and 32 (43%) patients had extensive colitis and left-sided colitis, respectively.

Comparison of dietary intake between patients and controls

The daily consumption of energy and nutrients of patients and controls is presented in Table 2. After adjusting for gender, age, body mass index, smoking status and energy intake, total protein intake and animal protein intake were respectively 2.76 g/d (95% CI 1.07–4.46) and 3.50 g/d (95% CI 1.67–5.34) higher among patients than controls, whereas no difference in vegetable protein intake was detected. Daily intake of carbohydrate was 10.1 g/d (95% CI 5.23–14.9) higher in patients compared with controls. Conversely, habitual intake of total fat, dietary fiber and alcohol was lower among patients than controls with a mean difference of −3.53 g/d (95% CI −5.57– −1.50), −2.19 g/d (95% CI −3.05– −1.32) and −2.38 g/d (95% CI −4.26– −0.50), respectively. Collectively, this resulted in a lower energy intake of −0.36 MJ/d (95% CI −0.70– −0.01) in patients compared with controls.

Table 1
General characteristics of inflammatory bowel disease patients and controls.

	Patients n = 165	Controls n = 1469	p-value
Female gender, n (%)	89 (54)	718 (49)	0.22
Age (years), median (IQR)	50 (40–57)	55 (45–62)	<0.01
Body mass index (kg/m^2), mean (SD)	24 (3.4)	26 (3.9)	<0.01
Smoking status, n (%)			
Never smoker	86 (52)	649 (44)	
Former smoker	53 (32)	510 (35)	
Current smoker	22 (13)	107 (7)	
Unknown	4 (2)	203 (14)	0.04
Educational level[a], n (%)			
Low	6 (4)	88 (6)	
Intermediate	69 (42)	571 (39)	
High	76 (46)	809 (55)	
Unknown	14 (9)	1 (0)	0.21

IQR: interquartile range; SD: standard deviation.
[a] Low educational level indicates no, primary or lower vocational education. Intermediate educational level indicates secondary or intermediate vocational education. High educational level indicates higher vocational or university education [39].

The daily food intake of patients and controls is listed in Table 3. In multivariable linear regression analyses, patients consumed more carbonated beverages and sugar and sweets than controls. Habitual intake of meat and poultry was also higher in patients compared with controls with an average difference of 15.0 g/d (95% CI 8.50–21.4) between the two groups. However, usual consumption of dairy products (except cheese) was −36.3 g/d (95% CI −65.8– −6.84) lower among patients as compared with controls. In addition, patients were found to have lower intakes of fruit and especially vegetables.

Associations of dietary intake with relapse in IBD patients

A total of 135 of 165 IBD patients (82%) were in clinical or endoscopic remission at baseline. During a median follow-up of 29 months (IQR 20–48 months), 41 of 135 patients (30%) developed a relapse. The median time between baseline and relapse was 14 months (IQR 6–23 months). Nineteen of 41 patients (46%) had active disease with a step-up in their medication. In another 19 (46%) patients disease activity was endoscopically confirmed. Two patients (5%) underwent surgery related to IBD and 1 patient (2%) was hospitalized due active IBD. Nondietary characteristics of IBD patients with and without relapse during follow-up are shown in Supplementary Table 2. Younger age (OR 0.96 per year, 95% CI 0.93–0.99) and the use of steroids (OR 19.1, 95% CI 2.27–161) or biologicals (OR 3.01, 95% CI 1.13–8.20) at baseline were associated with an increased risk of a relapse, whereas a higher body mass index (kg/m^2) was associated with a decreased risk of a relapse (OR 0.85 per 1 unit, 95% CI 0.75–0.97). Associations between macronutrient intake and relapse are presented in Table 4. A high intake of saturated fatty acid was found to be associated with a decreased risk of relapse after adjusting for gender, age and energy intake (OR 0.23, 95% CI 0.08–0.68). This inverse association was also detected with saturated fatty acid intake as a continuous variable in multivariable logistic regression analyses. Additionally, in continuous analyses, a reduced risk of developing a relapse was observed for total fat intake and intake of monounsaturated fatty acid with ORs of 0.63 (95% CI 0.44–0.91) and 0.37 (95% CI 0.15–0.91), respectively, while a positive association was found for dietary fiber intake (OR

Table 2
Daily nutrient intake[a] of inflammatory bowel disease patients and controls at baseline.

	Patients n = 165	Controls n = 1469	Beta (95% CI)
Energy (MJ)	8.33 (6.77–9.78)	8.56 (7.39–10.2)	−0.36 (−0.70– −0.01)[b]
Protein (g)	74.9 (61.5–85.8)	75.7 (64.0–88.0)	2.76 (1.07–4.46)[b]
Percent energy from protein	15.2 (13.8–17.1)	14.8 (13.4–16.2)	0.63 (0.28–0.98)[b]
Animal protein	41.0 (33.5–50.6)	40.6 (32.5–49.5)	3.50 (1.67–5.34)[b]
Vegetable protein	32.1 (25.4–40.1)	34.3 (28.1–41.3)	−0.76 (−1.84–0.32)
Fat (g)	72.4 (61.6–90.3)	80.9 (65.6–101)	−3.53 (−5.57– −1.50)[b]
Percent energy from fat	33.9 (30.4–37.1)	35.9 (32.4–39.4)	−1.73 (−2.62– −0.83)[b]
Saturated fatty acid	25.6 (21.2–31.9)	27.5 (21.5–34.9)	−0.04 (−1.04–0.97)
Monounsaturated fatty acid	24.9 (21.0–31.9)	29.0 (23.4–36.6)	−2.50 (−3.41– −1.58)[b]
Polyunsaturated fatty acid	15.4 (12.1–18.8)	17.0 (13.2–21.9)	−0.93 (−1.67– −0.19)[b]
n-3 polyunsaturated fatty acid	1.87 (1.49–2.38)	2.14 (1.68–2.69)	−0.10 (−0.21–0.01)
n-6 polyunsaturated fatty acid	12.4 (9.53–15.7)	14.1 (10.9–18.5)	−0.98 (−1.6– −0.32)[b]
n-6/n-3 ratio	6.45 (5.76–7.40)	6.60 (5.77–7.54)	−0.16 (−0.42–0.10)
Carbohydrate (g)	221 (182–267)	219 (181–266)	10.1 (5.23–14.9)[b]
Percent energy from carbohydrate	45.7 (42.0–50.3)	43.8 (40.0–47.5)	2.12 (1.21–3.04)[b]
Mono- and disaccharide	91.1 (73.8–117)	95.1 (74.4–117)	5.01 (0.74–9.28)[b]
Polysaccharide	124 (101–154)	125 (100–155)	5.06 (1.39–8.72)[b]
Dietary fiber (g)	21.5 (17.2–25.3)	24.1 (20.2–28.9)	−2.19 (−3.05– −1.32)[b]
Percent energy from fiber	2.08 (1.81–2.37)	2.20 (1.92–2.58)	−0.21 (−0.30– −0.13)[b]
Alcohol (g)	4.06 (0.86–11.7)	7.84 (1.73–16.5)	−2.38 (−4.26– −0.50)[b]
Percent energy from alcohol	1.46 (0.30–4.06)	2.62 (0.58–5.37)	−0.84 (−1.46– −0.22)[b]

CI: confidence interval.
Regression coefficient beta indicates the average difference in dietary intake between patients and controls adjusted for gender, age, body mass index, smoking status and energy intake. Betas presented for energy intake and percent of energy from various dietary intakes were not adjusted for energy intake.
[a] Daily intakes are displayed as median (interquartile range).
[b] p-value lower than 0.05.

Table 3
Daily food intake[a] of inflammatory bowel disease patients and controls at baseline.

	Patients n = 165	Controls n = 1469	Beta (95% CI)
Carbonated beverages (g)	21.0 (0.00–95.9)	8.81 (0.00–48.1)	0.78 (0.33–1.24)[b,c]
Coffee/tea (g)	696 (479–813)	688 (527–890)	−44.5 (−98.5–9.43)
Dairy products (g)	258 (153–396)	315 (200–446)	−32.8 (−62.1– −3.51)[c]
Milk products (except cheese)	236 (131–368)	290 (167–419)	−36.3 (−65.8– −6.84)[c]
Cheese	22.7 (8.55–44.3)	23.9 (12.3–40.2)	−0.02 (−0.26–0.23)[b]
Fats/oils/savory sauce (g)	40.3 (27.9–57.0)	44.3 (30.9–58.3)	−0.35 (−3.06–2.37)
Fruits/vegetables (g)	235 (126–324)	339 (224–440)	−0.58 (−0.72– −0.45)[b,c]
Fruits	157 (80.5–226)	212 (83.0–238)	−17.6 (−37.8–2.60)
Vegetables	60.9 (41.0–94.6)	148 (95.8–200)	−1.13 (−1.27– −0.99)[b,c]
Grains (g)	56.0 (33.1–87.4)	54.9 (32.5–93.6)	−0.10 (−0.30–0.11)[b]
Meats, poultry and fish (g)	92.8 (70.3–124)	83.7 (59.5–109)	16.4 (9.76–23.0)[c]
Meats and poultry	75.8 (53.2–108)	66.5 (39.4–93.0)	15.0 (8.50–21.4)[c]
Fish	11.7 (7.68–17.9)	14.9 (9.21–16.5)	1.42 (−0.94–3.79)
Sugar and sweets (g)	30.8 (16.1–51.2)	25.7 (12.7–43.9)	0.36 (0.16–0.56)[b]

CI: confidence interval.
Regression coefficient beta indicates the average difference in dietary intake between patients and controls adjusted for gender, age, body mass index, smoking status and energy intake.
[a] Daily intakes are displayed as median (interquartile range).
[b] The dependent variable was $\log_2$-transformed.
[c] p-value lower than 0.05.

3.65, 95% CI 1.44–9.26). Higher total carbohydrate intake also appeared to be predictive of a relapse, although this was not statistically significant (OR 1.14, 95% CI 0.99–1.30). Additional adjustment for either body mass index, smoking status, steroid or biological use did not considerably change the effect sizes (data not shown).

Discussion

In this study, patients with IBD were found to have higher dietary intakes of (animal) protein and carbohydrate and lower intakes of (unsaturated) fat, dietary fiber and alcohol compared with individuals from a general Dutch population. This appeared mainly due to higher consumption of carbonated beverages, meat and poultry and sugar and sweets, and lower consumption of dairy products (except cheese), fruit and vegetables by IBD patients than controls. Furthermore, several dietary factors, particularly (saturated) fat and fiber, seemed to be associated with a relapse during follow-up. Together, these data indicate that dietary intakes of IBD patients with longstanding but presently quiescent disease are different from those of the general population and may have a role in disease course. This underscores the need for further studies to assess the impact of these differences on general and intestinal health.

Most nutritional observational studies have been aimed at examining associations of diet with the development of IBD [10]. However, dietary intakes of IBD patients with longstanding disease and a comparison with individuals from the general populations

Table 4
Association between macronutrient intake and relapse at follow-up among inflammatory bowel disease patients.

	Median daily intake (IQR)		Categorical analysis		Continuous analysis
	Relapse n = 41	No relapse n = 94	Low intake OR	High intake OR (95% CI)	OR (95% CI)
Energy (MJ)	8.10 (6.54–88.0)	8.56 (6.81–10.0)	1.00	0.63 (0.28–1.42)	0.86 (0.69–1.05)
Protein (g)	74.5 (59.5–83.4)	75.4 (62.9–86.1)	1.00	2.01 (0.70–5.81)	1.28 (0.90–1.81)
Fat (g)	68.5 (60.1–78.8)	74.0 (63.4–93.8)	1.00	0.40 (0.13–1.23)	0.63 (0.44–0.91)[a]
Saturated fatty acid	23.6 (19.8–27.1)	27.3 (21.8–33.8)	1.00	0.23 (0.08–0.68)[a]	0.27 (0.11–0.63)[a]
Monounsaturated fatty acid	23.0 (20.4–28.7)	25.6 (21.7–34.0)	1.00	0.55 (0.20–1.51)	0.37 (0.15–0.91)[a]
Polyunsaturated fatty acids	15.3 (12.4–17.4)	15.7 (12.3–19.9)	1.00	0.73 (0.30–1.81)	0.98 (0.40–2.40)
n-3 polyunsaturated fatty acids	1.76 (1.49–2.18)	1.91 (1.52–2.54)	1.00	0.82 (0.34–1.96)	0.95 (0.50–1.78)
n-6 polyunsaturated fatty acids	12.7 (10.0–15.0)	12.7 (9.45–16.4)	1.00	1.09 (0.45–2.66)	1.05 (0.91–1.11)
n-6/n-3 ratio	6.48 (5.62–7.94)	6.35 (5.75–7.31)	1.00	1.01 (0.46–2.20)	1.08 (0.83–1.40)
Carbohydrate (g)	223 (184–256)	221 (182–279)	1.00	2.06 (0.67–6.31)	1.14 (0.99–1.30)
Dietary fiber (g)	21.3 (16.9–25.9)	21.5 (17.4–24.9)	1.00	1.68 (0.65–4.36)	3.65 (1.44–9.26)[a]
Alcohol (g)	2.26 (0.03–7.32)	4.93 (1.45–13.2)	1.00	0.58 (0.26–1.30)	0.98 (0.94–1.03)

CI: confidence interval; IQR: interquartile range; OR: odds ratio.
ORs are adjusted for gender, age and energy intake, except for ORs presented for energy intake (adjustment only for gender and age). ORs are presented for increment of 10 units of dietary variable, apart from energy intake and alcohol consumption (ORs per 1 unit).
[a] p-value lower than 0.05.

have not been extensively assessed. Despite a lack of data supporting a specific diet in individuals with CD or UC, IBD patients frequently believe that diet is a risk factor for a relapse and report adjusting their dietary intake accordingly [4–7]. The reduced consumption of fat, alcohol, dairy products, fruit and vegetables found in this study is in line with previous studies on dietary beliefs among IBD patients reporting that these foods were often perceived as triggers for relapse or worsened symptoms [4–7]. Furthermore, apart from a low intake of (unsaturated) fat, these results seem to substantiate studies focusing on preillness diet [10]. In previous prospective cohort studies, individuals with incident CD and UC were found to have a high protein intake, specifically animal protein, and a low intake of dietary fiber before diagnosis [27,28]. This may suggest that general food patterns of IBD patients persist after diagnosis. Similar results were reported in a study comparing dietary intakes of patients with established UC with recommended dietary values [9]. Some dietary intakes of patients in the present study did not appear to meet common dietary recommendations for the general public [29]. IBD patients, for example, consumed over twice as little vegetables as individuals from the general population. It should be noted that the average differences in dietary intake between groups were sometimes statistically significant but mostly small and its clinical consequences are uncertain. Nonetheless, these differences possibly impact general health and prompt further interest.

Relatively few studies have investigated associations of usual dietary intake with disease course in patients with established CD or UC and generated different findings [11,12]. In two previous studies in UC patients, foods rich in sulfur and sulfate, such as meat and alcohol, were associated with active disease [13,30]. These compounds have been suggested to have direct toxic effects on colonocytes and increase intestinal permeability [13]. However, a recent study in UC patients was unable to replicate these findings [31]. Associations with sulfur and sulfate rich foods could also not be demonstrated in the present study, possibly due to a different selection of foods or because both CD and UC patients were included. Most notably, assessment of the amount of sulfur and sulfate intake was not possible. The role of fatty acids in IBD has also received interest. A cross-sectional study in CD patients reported an association between a high intake of total, saturated, and monounsaturated fat, as well as a higher ratio of n-6 polyunsaturated fatty acids to n-3 polyunsaturated fatty acids, and active disease [14,32]. Associations with these nutrients were not observed in the present study, which might result from a different methodological design. Cross-sectional investigations carry an inherent risk of reverse causation. Furthermore, opposing results have also been reported [33]. Finally, in a recent prospective study, high consumption of dietary fiber was found to reduce the risk of relapse among CD patients [16], whereas a positive association between intake of fiber and relapse risk was detected in the present study. Dietary fibers can be fermented to short chain fatty acids, which are assumed to have anti-inflammatory effects [34]. However, there are only poor clinical data supporting the efficacy of fiber in improving disease outcomes [35], and negative effects of fiber have also been observed [36]. Of note, there is a wide spectrum of dietary fibers and generation of short-chain fatty acids from bacterial fermentation depends on specific types of fiber. Since only total fiber intake was investigated, differential effects of specific fibers could not be determined. Overall, considering the limited number of studies and the lack of coherent associations, definitive dietary recommendations for IBD patients cannot be made at this moment.

Several limitations of this study merit consideration. IBD patients were identified from subjects undergoing endoscopic surveillance for colorectal cancer. Consequently, patients often had longstanding disease with a history of colonic involvement. This might reduce the external validity of the findings. On the other hand, the availability of endoscopic data provided the opportunity to study the association between dietary intake and the development of relapse in patients who were truly in remission when completing the FFQ, thereby reducing the risk of reverse causation. Although participants of the NQplus study showed similarities with the general Dutch population, participants were less frequently smokers and received a relatively higher level of education, potentially compromising the appropriateness of the comparison group. Dietary assessment included the use of FFQs that were self-completed and captured only intake of the preceding month, which may carry the risk of misclassification. Seasonal influences may have been missed. However, recalls were almost equally distributed across the seasons of the year and seasonal variation of the availability of foods is generally limited in western countries. Moreover, an advantage of using one-month questionnaires includes the limited risk of recall bias. Dietary intake was assessed once and it cannot be ruled out that patients changed their diets during follow-up, although data have shown that general food patterns of (healthy) individuals remain relatively stable over time and the aim was to assess patient's diet during disease remission [37]. Assessment of development of relapses was based on review of medical records rather than the structural use of validated clinical disease

activity indices. However, the endpoints used for relapse were clearly defined and do reflect clinically evident and relevant disease activity. Moreover, in approximately half of patients, active disease was endoscopically confirmed. The relatively limited number of patients with a relapse restricted the possibility to study associations for CD and UC separately or according to distribution of disease. Lastly, outcomes of multiple dietary variables were examined, which may carry the risk of false positive findings. However, the variables that were investigated were selected based on previous studies and differences found in this study appeared to be in line with dietary patterns that were previously observed [38].

There were several strengths to this study. First, a relatively large sample of IBD patients and unaffected individuals from the general Dutch population was included. Second, for most IBD patients, endoscopic data were available to accurately assess the presence of active disease at baseline. Third, a comprehensive FFQ was used for the assessment of habitual dietary intake. Finally, associations between usual diet and disease course were examined longitudinally by assessing the development of disease relapses after measuring dietary intake.

In conclusion, this study showed that patients with IBD had higher dietary intakes of (animal) protein and carbohydrate and lower intakes of (unsaturated) fat, dietary fiber and alcohol than individuals from a general Dutch population. The results further underscore that dietary factors, particularly (saturated) fat and fiber, may have a role in disease course. Since diet is a potentially modifiable risk factor, future studies should investigate the impact of dietary factors on disease course and general health in patients with IBD.

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Disclosures

No potential conflicts relevant to this manuscript.

Author contributions

Conception and design of the study: JLO, BO, BJMW; acquisition of data, or analysis and interpretation of data: JLO, JHdV, AW; critical revision of the manuscript important intellectual content: all authors; final approval of the version to be submitted: all authors.

Conflict of interest

None.

Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.clnu.2018.06.983.

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