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Avoidance of Fiber is Associated with Greater Risk of Crohn's Disease Flare in a 6 Month Period

Carol S. Brotherton, PhD[1], **Christopher A. Martin, MSPH**[2,3], **Millie D. Long, MD, MPH**[2,3], **Michael D. Kappelman, MD, MPH**[2,4], and **Robert S. Sandler, MD, MPH**[2,3]

[1]School of Nursing, George Mason University, Fairfax, VA

[2]Center for Gastrointestinal Biology and Disease, University of North Carolina, Chapel Hill, NC

[3]Department of Medicine, University of North Carolina, Chapel Hill, NC

[4]Department of Pediatrics, University of North Carolina, Chapel Hill, NC

Abstract

Background & Aims—Chronic inflammatory bowel diseases (IBDs) have been associated with an abnormal mucosal response to the gastrointestinal microbiota. Although dietary fiber affects the gastrointestinal microbiota, there is limited information on the role of fiber on IBD activity. We investigated factors associated with fiber consumption and whether it was associated with flares in patients with IBD.

Methods—We collected a completed 26-item dietary survey from 1619 participants in the Crohn's and Colitis Foundation of America Partners Internet cohort (Crohn's disease, 1130; ulcerative colitis/indeterminate colitis, 489). Eligible individuals were in remission based on disease activity index at baseline and completed a follow-up survey 6 months later. Fiber and whole grain consumption were categorized into quartiles and deciles. Disease flare at 6 months was defined as a disease activity index score exceeding remission cut-off values, and/or an IBD-related surgical procedure or hospitalization since baseline.

Results—Participants with longer duration of disease, past history of surgery and past IBD hospitalization ate less fiber. The risks for disease flare differed by disease type. Compared to those in the lowest quartile of fiber consumption, participants with Crohn's disease in the highest quartile were less likely to have a flare (adjusted odds ratios [OR], 0.58, 95% confidence interval [CI], 0.37–0.90). Participants with Crohn's disease who reported that they did not avoid high fiber foods were ~40% less likely to have a disease flare than those who avoided high fiber foods

Correspondence Author: Carol S. Brotherton, PhD, 5413 Tree Line Drive, Centreville, VA 20120, Phone: 1-703-282-1656, csb8b@virginia.edu.

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(adjusted OR, 0.59; 95% CI, 0.43–0.81). There was no association between fiber intake and flares in patients with ulcerative colitis (adjusted OR, 1.82; 95% CI, 0.92–3.60).

Conclusions—Intake of dietary fiber is associated with reduced disease flares in patients with Crohn's disease, but not UC. Recommendations to limit dietary fiber should be reevaluated.

Keywords

inflammatory bowel disease; diet; microbiota; dysbiosis; short-chain fatty acids; food; CD; UC

BACKGROUND

Crohn's disease (CD) and ulcerative colitis (UC) are chronic inflammatory bowel diseases (IBDs) that can have a significant impact on quality of life. IBD is thought to result from an abnormal mucosal immune response to commensal gut bacteria in genetically susceptible individuals. Diet, particularly dietary fiber, can influence the gastrointestinal microbiota and potentially impact IBD course.

Information on the role of dietary fiber in the treatment and maintenance of IBD is limited despite more than 3 decades of study. A systematic review identified 23 randomized controlled trials that provided weak evidence of benefit.[1] The studies were typically small and of short duration. Although there are reasons to think that fiber could have a beneficial influence through generation of short chain fatty acids such as butyrate, patients with IBD are often instructed to limit their fiber consumption.

We took advantage of dietary information provided by a large number of IBD participants enrolled in an Internet-based cohort study to explore the effect of self-reported dietary fiber consumption on disease activity. We sought to describe demographic and disease related factors associated with baseline fiber consumption and determine whether fiber consumption would predict disease flare at 6 months.

METHODS

Data were derived from the Crohn's and Colitis Foundation of America (CCFA) Partners Study. CCFA Partners is a longitudinal Internet-based cohort of more than 14,000 participants with IBD. The development of the cohort has been described in detail previously.[2] Briefly, individuals with IBD who were older than 18 years of age were recruited to join CCFA Partners using CCFA email rosters, social media, educational and fundraising events and the CCFA Website. Each participant completed a baseline survey that contained questions about demographic characteristics, treatments, disease duration, and disease activity. Follow-up surveys have been completed every six months to capture changes in disease activity and treatment since the prior survey. A randomly selected subset of participants completed an optional survey module about diet at initial enrollment. The study population for the current analysis is comprised of members of the CCFA Partners cohort who completed the baseline dietary survey module, were in remission at baseline, and subsequently completed a six-month follow-up survey.

The dietary survey used for this study was a 26-item validated Dietary Screener Questionnaire (DSQ) that was developed by the Risk Factor Monitoring and Methods Branch of the National Cancer Institute (NCI).[3–5] The survey asks about the frequency of consumption in the past month of selected foods and drinks. Comparing the screener to multiple 24-hour recalls, correlation coefficients for fiber intake range from 0.54 to 0.55 for women and from 0.52 to 0.60 for men.[5] For the current analyses we used algorithms developed by the NCI for use with the DSQ to calculate consumption of whole grains and fiber. Fiber and whole grain consumption were categorized into quartiles and deciles.

Disease activity was classified using the Short Crohn's Disease Activity Index (sCDAI)[6] and the Simple Clinical Colitis Activity Index (SCCAI).[7] Remission was defined as sCDAI score <150 or a SCCAI ≤2. Disease flare at 6 months was defined as a disease activity index score exceeding the cut-off for remission, and/or the need for an IBD-related surgical procedure or IBD-related hospitalization during the 6-month follow-up period. Pre-baseline history of IBD surgery and hospitalization were dichotomous variables. Indeterminate colitis was grouped with ulcerative colitis for these analyses.

All statistical analyses were performed using SAS version 9.3 (Cary, NC). Categorical variables were expressed as proportions and compared using chi square tests. Logistic regression models were used to predict disease flare at 6 months. We assessed possible effect modification by disease type (CD versus UC/IC). Potential confounders were selected using change-in-estimate methods and a priori knowledge. The study was approved by the Institutional Review Board of the University of North Carolina, Chapel Hill.

RESULTS

A total of 1619 adults in remission at baseline completed a diet survey and a 6-month follow-up survey (Crohn's disease, 1130; ulcerative colitis/indeterminate colitis, 489). Demographic and descriptive characteristics of the study population are shown in Table 1. Participant ages were distributed throughout all adult decades of life. Half (50.1%) of participants reported a disease duration of 11 years or greater.

We compared the characteristics of participants in the top versus bottom quartiles of fiber consumption [Table 2]. UC and male gender were strongly associated with higher fiber consumption, specifically participants with UC were 2.6 times more likely to be in the highest quartile of fiber consumption when compared to participants with CD, OR 2.63 (95% CI 1.91–3.62). Men were almost 5 times more likely than women to be high fiber consumers, OR 4.74 (95% CI 3.34–6.73). Overall, there was no difference in fiber consumption by age, weight, or flare at 6 months, with flare at follow- up based on disease activity index alone, or with a broader definition of flare that included hospitalization or IBD surgery between baseline and follow-up surveys. Participants with longer duration of disease, past history of surgery or past hospitalization for IBD ate less fiber. Current IBD medication use was not related to fiber consumption.

Disease flare was defined as participants who were no longer in remission based on disease activity index at follow-up, or who required IBD-related hospitalization or surgery between

baseline and follow-up. Table 3 shows ORs for flare at 6 months, stratified by disease type. Among CD participants, those in the highest quartile of fiber were significantly less likely to have a flare, crude OR 0.57 (95% CI 0.38–0.86). After adjusting for sex, age, previous history of surgery or hospitalization, duration of disease and body weight, results were similar, adjusted OR 0.58 (95% CI 0.37–0.90). We compared each quartile to the lowest quartile to be certain that the fourth quartile results were not anomalous. For CD the point estimates for quartiles 2 and 3 were intermediate between the reference and quartile 4. For UC the trends were less clear but were generally consistent with the data presented in Table 3.

To see if a more extreme value of high fiber might be protective, we compared the top 10% (decile) to the lowest decile. The effect size was more pronounced than the quartile analysis, adjusted OR 0.37 (95% CI 0.16–0.85). Results were similar for whole grain consumption, with highest quartile whole grain consumers significantly less likely to flare, crude OR 0.62 (95% CI 0.41–0.94), adjusted OR 0.66 (95% CI 0.43–1.01) To be certain that patients categorized as in remission at baseline did not have a flare shortly prior to enrollment or were not maintained in remission by steroids, we conducted a sensitivity analysis that excluded any patient on steroids at baseline or who had an IBD hospitalization during the 12 months prior to baseline. The results were unchanged.

In contrast, among UC/IC patients, effect estimates suggested that high fiber consumption was not associated with the likelihood of flare, with crude and adjusted ORs for quartile 4-versus-1 of 1.38 (95% CI 0.74–2.60) and 1.82 (95% CI 0.92–3.60) respectively. The effect was greater when comparing the highest and lowest deciles, adjusted OR 4.78 (95% CI 1.05–21.66). Whole grain consumption among UC patients had a similar relationship, with adjusted ORs for flare of 1.25 (95% CI 0.68–2.31) for the quartile-based analysis, and an imprecise but significant OR 3.29 (95% CI1.02–10.59) for decile-based analysis.

The Diet Screener Questionnaire used for this analysis asked participants to indicate the specific brand of cereals consumed, from a list of over 300 brands. We identified the seven cereals with the highest fiber content (“ultra-high fiber bran cereals”). Only 10 persons (0.62%) reported using any of the 7 ultra-high fiber bran cereals; 7 of these 10 were in the top quartile of fiber intake, and 5 of 10 were in the top decile. The proportion of ultra-high fiber bran cereal users was similar in CD versus UC participants. Our survey also included questions about avoidance of certain types of foods, including “high fiber foods”. There were 479 (29.6%) participants who said they avoided high fiber foods; none of these were ultra-high fiber bran cereal users. Compared to fiber avoiders, the small number (10) of ultra-high fiber bran cereal users were less than half as likely to flare, adjusted OR 0.42 (95% CI 0.05–3.72). Additionally, CD participants who reported that they did not avoid high-fiber foods were about 40% lower likelihood of flare than those who avoided high fiber foods, adjusted OR 0.59 (95% CI 0.43–0.81).

We assessed possible effect modification of the association between fiber intake and flare across strata of each covariate: IBD subtype, sex, history of IBD hospitalization and surgery, duration of disease and age. We found an effect modification by disease subtype (CD, UC/IC), and therefore reported all results stratified by IBD subtype. We did not observe effect

modification, qualitatively or statistically, for age, sex, history of IBD hospitalization and surgery, or duration of disease, thus did not report stratum-specific effects for these variables.

DISCUSSION

The present study found striking differences in fiber consumption by disease type – UC participants consumed more fiber than did participants with CD. Female gender, prior hospitalization and prior surgery were all associated with lower fiber intake. The relationship between fiber consumption and flare at follow-up differed between CD and UC participants; the highest quartile fiber consumption was associated with a 40% lower odds of disease flare at 6 months among CD participants, whereas fiber intake amongst UC participants had no significant association with disease flare at 6 months. Some adjusted estimates for ulcerative colitis suggested that fiber increased the risk of flare. Because these were based on small numbers, the confidence intervals are very wide and the point estimates unstable.

The fiber intake in our population is similar to that of the US population. NHANES 2009–2010 reports fiber intake as approximately 17 g/day among adults. A 2012 publication reports mean fiber intake for adults as 15.9 g/day for 2008.[8] In our study population intake is comparable, with overall mean fiber intake of 16.1 and 18.0 g/day for CD and UC, respectively. The means in the highest quartiles was considerably higher, with means of 23.7 (CD) and 24.5 (UC).

Since at least the 1970s, researchers have hypothesized that the lack of dietary fiber in industrialized diets is an important factor in the emergence of IBD.[9] Recent technological advancements, such as culture-independent characterization of microbes, have increased the scientific understanding of gut microbiota[10] and shown the relevance of dysbiosis to IBD.[11] Scientists worldwide are testing the therapeutic use of dietary fiber to improve gut function in IBD by affecting microbial balance and increasing fiber metabolites (short-chain fatty acids).[12–23] Whereas most prior research focused on fiber supplements, the Partners data supports the idea that the fiber content of everyday foods may be an important variable in IBD disease course.

In 1979, Heaton et al. analyzed outcomes of 32 patients with CD who were treated for a mean of 4 years with a fiber-rich, unrefined carbohydrate diet in addition to conventional management, comparing outcomes with those of 32 matched patients with CD who received no dietary instruction. Similar to our findings in CD, Heaton et al. found that the higher fiber group had fewer hospitalizations than the group receiving no diet instruction (11 hospitalizations and 34 hospitalizations, respectively; $P < 0.01$). The high fiber group had fewer surgeries and spent fewer days in the hospital than the group that received no dietary instruction, even excluding hospitalizations due to surgeries (80 days in the high fiber group; 414 days in the group with no diet instruction; $P < 0.01$). Incidentally, Heaton et al. (1979)[24] reported that in all of their combined 150 patient years of recommending a fiber-rich diet for CD, no patient developed obstructions, despite the fact that many of their patients had a previous history of strictures before starting a fiber-rich pattern of eating.

It is not clear whether the lower fiber consumption in CD participants in the present study is the result of physician instructions or participant preference. Participants with stricturing disease may avoid fiber because they encounter symptoms, particularly bloating, when they eat certain fibrous foods. It is possible that patients with strictures might avoid fiber to prevent obstructive symptoms. If they flared in the next 6 months we would erroneously attribute the flare to fiber avoidance. Because we did not have accurate information on disease phenotype we cannot exclude that possibility. Conversely, it may be that post-surgical participants continued with a low fiber diet after it was warranted, because they received little post-operative nutritional counseling.

Few participants in this sample consumed ultra-high fiber bran cereal. Although consumer demand has kept *All Bran®* cereals on U.S. grocery store shelves since 1916,[25] only 25 out of 3,274 (<1%) Partners participants who answered the questions about cereal brands reported consuming *All Bran®* or any similar cereals. Also, we have documented in this large sample that 30% of participants avoid dietary fiber altogether. It is unknown how much of this fiber restriction is caused by medical necessity and how much is caused by incomplete and imbalanced fiber information favoring reduction of fiber for individuals with IBD.

We observed that the risk of flare at 6 months differed by IBD type. This differential effect is not unexpected, and in fact, the effect of many environmental exposures on IBD outcomes are different for CD and UC. Smoking is perhaps the most-studied example. Smoking is a clear risk factor for CD relapse and post-operative recurrence; however, it may have a protective effect for patients with UC.[26]

Among CD participants, the higher rate of flares at 6 months for fiber avoiders versus non-avoiders suggests a need for further research. Important questions remain regarding the underlying cause of dietary fiber restriction as well as the effect of dietary fiber in individuals with gut pathophysiology characteristic of IBD. First, it is unknown if the association between fiber restriction and increased disease activity represents a causal relationship. Second, if there is a causal relationship, it is unknown which came first. Participants in the study who avoid fiber may have been destined to have problems due to more aggressive disease phenotypes with significant stricturing that causes them to avoid fiber. In contrast, plausible mechanisms published in support of fiber for CD research[27] could explain the significantly lower disease activity found in the group that did not avoid fiber.

Our study has limitations. The dietary information was obtained by a short validated screener.[4, 5] It is possible that the fiber intake was measured inaccurately. We believe that any misclassification of fiber intake was random which would bias the study toward the null. Despite the large size of the study, the numbers of participants in certain subgroups was limited. We do not have accurate information from this Internet survey about disease phenotype, particularly stricturing disease in CD. However, in sensitivity analyses among CD patients, effect estimates were very similar after excluding those with any history of IBD surgery or hospitalization, suggesting that our observations of protective effects of fiber intake on flare was not influenced by aggressive phenotypes. The survey was not designed to

test the fiber hypothesis, and for that reason there were not detailed questions about specific fiber types. We defined 'flare' as participants with an elevated disease activity index, hospitalization or surgery at the 6-month follow-up. It is possible that participants were beginning to flare at baseline and changed their diet as a consequence. There were only a small number of participants who ate ultra-high fiber bran cereals, therefore limiting these subgroup analyses. Although this study is strengthened by its prospective design over a 6 month follow-up, compared to the progression of IBD disease activity over many years, the follow-up period of this study is limited.

The results of this study support findings reported in investigations occurring in the 1980s – low fiber eating does not result in improved outcomes for individuals with CD compared to individuals with CD not restricting fiber intake.[28, 29] More research is needed to explore the causes of fiber restriction in CD. More prospective studies are needed to explore the potential benefits of fiber-containing foods in the diet of individuals with IBD, especially in specific phenotypes. As suggested by the authors of a recent IBD diet review,[30] it is unlikely that a single diet will be found to be sufficient to manage all IBD phenotypes; however, it will be remarkable progress if a diet is found to be sufficient alone for some and adjunctive therapy for others.

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Abbreviations used in this paper

CI	confidence intervals
CCFA	Crohn's and Colitis Foundation of America
DSQ	Dietary Screener Questionnaire
CD	Crohn's disease
NCI	National Cancer Institute
OR	odds ratio
SCCAI	Simple Clinical Colitis Activity Index
sCDAI	Short Crohn's Disease Activity Index
UC	ulcerative colitis

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Table 1

Characteristics of the study population

N = 1619	Stratum	Crohns n = 1130	Ulcerative colitis n = 489
Sex, n (%)	Male	338 (29.9)	151 (30.9)
	female	792 (70.1)	338 (69.1)
Age category, n (%)	<=30	246 (21.8)	112 (22.9)
	31–40	241 (21.3)	98 (20.0)
	41–50	202 (17.9)	105 (21.5)
	51–60	252 (22.3)	87 (17.8)
	>60	189 (16.7)	87 (17.8)
Duration of disease, n (%)	0–1 yr	81 (7.2)	40 (8.2)
	02–5 yrs	227 (20.1)	114 (23.4)
	06–10 yrs	223 (19.8)	122 (25.0)
	11–20 yrs	280 (24.8)	120 (24.6)
	>20 yrs	316 (28.0)	92 (18.9)
History of surgery, n (%)	No	615 (54.4)	472 (96.5)
	Yes	515 (45.6)	17 (3.5)
History of hospitalization, n (%)	No	349 (30.9)	306 (62.6)
	Yes	781 (69.1)	183 (37.4)
Fiber intake, g/day			
Mean (std)		16.0 (6.5)	18.0 (7.4)
Median (IQR)		14.6 (11.6–18.6)	16.1 (13.3–21.1)
Whole grain intake, oz eq/day			
Mean (std)		1.0 (1.4)	1.3 (1.6)
Median (IQR)		0.6 (0.2–1.2)	0.8 (0.3–1.6)
Flare at follow-up			
Total flare (sCDAI/SCAI or hospitalized/surgery)	No	877 (77.6)	354 (72.4)
	Yes	253 (22.4)	135 (27.6)
Defined by sCDAI/SCAI	No	927 (82.0)	365 (74.6)
	Yes	203 (18.0)	124 (25.4)
# hospitalized or surgery	No	1080 (95.6)	478 (97.8)
	Yes	50 (4.4)	11 (2.2)
Median (IQR) baseline disease activity scores, sCDAI (Crohns) or SCAI (UC)		79 (58,107)	1 (1,2)
Quartile of body weight	Q1: 85–130 lbs	283 (25.1)	138 (28.2)
	Q2: 131–152 lbs	276 (24.4)	118 (24.1)
	Q3: 153–180 lbs	303 (26.8)	119 (24.3)
	Q4: 180.4–353 lbs	267 (23.6)	114 (23.3)
Current use of steroids	No	1065 (94.2)	464 (94.9)
	Yes	65 (5.8)	25 (5.1)
Current use of immunosuppressants	No	200 (35.0)	66 (35.7)
	Yes	372 (65.0)	119 (64.3)
Current use of aminosalicylates	No	200 (30.8)	66 (15.4)

N = 1619	Stratum	Crohns n = 1130	Ulcerative colitis n = 489
	Yes	450 (69.2)	363 (84.6)
Current use of biologics	No	200 (32.0)	66 (44.6)
	Yes	425 (68.0)	82 (55.4)

Table 2

Associations of quartiles of fiber consumption by characteristics of study participants

Characteristic	Stratum	N	Fiber quartile_1 (N=404)	Fiber quartile_4 (N=405)	Odds ratio (95% CI)
Disease type	CD	577	327 (56.7)	250 (43.3)	ref
	UC/IC	232	77 (33.2)	155 (66.8)	2.63 (1.91–3.62)
Gender	female	587	351 (59.8)	236 (40.2)	ref
	male	222	53 (23.9)	169 (76.1)	4.74 (3.34–6.73)
Age category	<=30	167	77 (46.1)	90 (53.9)	ref
	31–40	178	90 (50.6)	88 (49.4)	0.84 (0.55–1.28)
	41–50	163	90 (55.2)	73 (44.8)	0.69 (0.45–1.07)
	51–60	182	88 (48.4)	94 (51.6)	0.91 (0.60–1.39)
	>60	119	59 (49.6)	60 (50.4)	0.87 (0.54–1.39)
Duration of disease	0–1 yr	68	43 (63.2)	25 (36.8)	ref
	2–5 yrs	174	79 (45.4)	95 (54.6)	2.07 (1.16–3.68)
	6–10 yrs	175	84 (48.0)	91 (52.0)	1.86 (1.05–3.31)
	11–20 yrs	192	83 (43.2)	109 (56.8)	2.26 (1.28–3.99)
	>20 yrs	198	113 (57.1)	85 (42.9)	1.29 (0.73–2.28)
History of surgery	no	539	250 (46.4)	289 (53.6)	ref
	yes	270	154 (57.0)	116 (43.0)	0.65 (0.49–0.87)
History of hospitalization	no	337	148 (43.9)	189 (56.1)	ref
	yes	472	256 (54.2)	216 (45.8)	0.66 (0.50–0.88)
Flare at follow-up	no	646	321 (49.7)	325 (50.3)	ref
	yes	163	83 (50.9)	80 (49.1)	0.95 (0.68–1.34)
Flare or hospitalization/surgery at follow-up	no	612	297 (48.5)	315 (51.5)	ref
	yes	197	107 (54.3)	90 (45.7)	0.79 (0.57–1.09)
Quartile of body weight	Q1: 85–130 lbs	213	125 (58.7)	88 (41.3)	ref
	Q2: 131–152 lbs	199	102 (51.3)	97 (48.7)	1.35 (0.92–1.99)
	Q3: 153–180 lbs	214	95 (44.4)	119 (55.6)	1.78 (1.21–2.61)
	Q4: 180.4–353 lbs	182	81 (44.5)	101 (55.5)	1.77 (1.19–2.64)
IBD medications at baseline	none	143	75 (52.4)	68 (47.6)	ref
	steroids	81	45 (55.6)	36 (44.4)	0.88 (0.51–1.53)

Characteristic	Stratum	N	Fiber quartile_1 (N=404)	Fiber quartile_4 (N=405)	Odds ratio (95% CI)
	immunosuppressants	240	117 (48.8)	123 (51.3)	1.16 (0.77–1.75)
	aminosalicylates	399	193 (48.4)	206 (51.6)	1.18 (0.80–1.73)
	biologics	254	138 (54.3)	116 (45.7)	0.93 (0.61–1.40)

Table 3

Crude and adjusted[†] odds ratios (95% confidence interval) for flare[*] at follow up by type and levels of fiber intake

IBD Type	Effect*	# cases flare	Median Intake (fiber g/day, whole gr oz eq/day)	Crude OR [95% CI]	Adjusted OR [95% CI]
CD	Fiber_quartile 1	89	10.4	Ref	Ref
CD	Fiber_quartile 2	59	13.4	0.72 [0.49–1.05]	0.72 [0.49–1.06]
CD	Fiber_quartile 3	61	17.0	0.77 [0.53–1.11]	0.75 [0.51–1.10]
CD	Fiber quartile 4	44	23.7	0.57 [0.38–0.86]	0.57 [0.37–0.87]
CD	Whole grain_quartile 1	77	0.1	Ref	Ref
CD	Whole grain_quartile 2	71	0.4	1.02 [0.70–1.48]	1.00 [0.69–1.46]
CD	Whole grain_quartile 3	62	0.9	0.86 [0.59–1.27]	0.87 [0.59–1.28]
CD	Whole grain_quartile 4	43	2.0	0.62 [0.41–0.94]	0.63 [0.41–0.96]
UC/IC	Fiber_quartile 1	18	10.8	Ref	Ref
UC/IC	Fiber_quartile 2	31	13.7	1.22 [0.62–2.42]	1.22 [0.62–2.42]
UC/IC	Fiber_quartile 3	39	16.8	1.62 [0.83–3.17]	1.62 [0.83–3.17]
UC/IC	Fiber_quartile 4	46	24.5	1.59 [0.83–3.05]	1.59 [0.83–3.05]
UC/IC	Whole grain_quartile 1	26	0.1	Ref	ref
UC/IC	Whole grain_quartile 2	33	0.4	1.03 [0.55–1.91]	1.03 [0.55–1.91]
UC/IC	Whole grain_quartile 3	29	0.9	0.87 [0.46–1.63]	0.87 [0.46–1.63]
UC/IC	Whole grain_quartile 4	46	2.1	1.27 [0.71–2.30]	1.27 [0.71–2.30]

[†]adjusted for sex, history of surgery, history of hospitalization, duration of disease and age).

[*]flare defined as not in remission or hospitalization or surgery at the time of the follow-up survey