

Original Article

Dietary risk factors for inflammatory bowel disease in Shanghai: A case–control study

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Background and Objectives: Inflammatory bowel disease (IBD) is a multifactorial condition involving the complex interplay of genomics, microbiota, immunology, environment, and personal behaviors, particularly diet. **Methods and Study Design:** A case–control study in a tertiary referral hospital. Fifty patients with IBD and 50 controls without gastrointestinal diseases were enrolled consecutively from October 1, 2016, to December 31, 2017. Sociodemographic and Food Frequency Questionnaires (FFQs) were completed, and dietary risk factors for IBD were identified. **Results:** Six major foods were associated with the recurrent incidence of IBD ($p < 0.05$): chili, fish, milk, nuts, eggs, and fruit. Logistic regression analysis revealed that eating chili and drinking milk more than three times weekly increased the risk of relapse, as did eating fish and nuts one or two times weekly. Eating fruit more than once weekly reduced the risk of IBD. Fish, seafood, vegetables, nuts, beef, and fruit, along with a history of food allergy, were associated with a high risk of clinically recurrent IBD. Dietary patterns featuring seafood and nuts also increased the risk of relapse. **Conclusions:** The consumption of chili, milk, fish, and nuts beyond moderate weekly frequencies increased the risk of IBD, whereas fruit consumption was consistently protective against IBD development. Relapse susceptibility was also associated with a history of food allergy. Thus, IBD risk management can involve more personalized and less restrictive dietary patterns, as well as the enforcement of weekly dose thresholds. Uncertainty remains regarding association differentials between ulcerative colitis (UC) and Crohn's disease (CD).

Key Words: Crohn's disease, ulcerative colitis, recurrence, diet, risk factors

INTRODUCTION

IBD is a chronic inflammatory condition affecting the gastrointestinal tract. The global incidence and prevalence of IBD, which encompasses CD and UC, are increasing. In Mainland China, epidemiological evidence reveals increases in the incidence of this cluster of conditions of 1.80, 1.33, and 0.46/1,000,000 for IBD, UC, and CD, respectively. These rates remain lower than those in the West. However, considering China's large population, the total attributable disease burden of IBD is considerable and is probably underestimated.¹ A review article discussed 150,000 cases of IBD (of which 97% were UC cases) reported over the past 15 years. From 1991 to 2010, IBD cases increased from 76,530 to 266,394, denoting a 2.5-fold increase.² IBD has a multifactorial etiology involving genetic susceptibility and environmental triggers that stimulate an inflammatory response. A Western-style diet may predispose people to IBD.³ Shifts toward a Western-style diet may partially explain the increasing incidence of IBD in Taiwan.⁴ Malnutrition is a common feature of IBD, with nutritional interventions focused not only on correcting nutrient deficiencies but also on reducing disease activity and symptoms. Evidence-based dietary approaches and management strategies are warranted to address eating problems and their clinical consequenc-

es proactively. The fact that diet affects the pathogenesis and persistence of IBD has been well established. However, how dietary recommendations should be applied in clinical nutrition practice remains under debate.

In the IBD literature, interest in managing inflammation has grown, as has interest regarding its dietary determinants, especially with regard to the gut microbiome and intestinal barrier integrity. Clinical nutrition or feeding studies are demanding, and their designs are understandably open with regard to food interventions. Population-based cohort studies and observational studies have identified the protective effects conferred by certain dietary components against IBD, as well as the risk factors for IBD.^{5,6} A case–control study has suggested that vegetables and fruits are protective.⁷ The consumption of re-

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fined sugar and fat is a risk factor for IBD.⁸ In this case-control study, we examined the dietary risk factors for IBD through a FFQ administered to individuals living in Shanghai, where IBD incidence is increasing rapidly.

METHODS

Patient selection

We conducted this study at our tertiary referral center (Huadong Hospital, Fudan University) from October 2016 to December 2017, in a self-report questionnaire was administered. Eligible participants must have received diagnoses of UC or CD. We enrolled patients who presented to the outpatient or inpatient department of the hospital. The diagnostic criteria for UC and CD accorded with those proposed by the Inflammatory Bowel Disease Group in China.⁹ Controls were individuals without gastrointestinal diseases who were recruited from the physical examination center of the hospital during the same period. Individuals with cancers (other than those of lymphohematopoietic tissues), chronic bowel disease, acute appendicitis, allergic diseases, and anal fistulas were excluded. Controls were frequency matched with cases by sex and age (10-year age groups).

Disease activity

UC can be divided into primary and chronic relapsing UC.¹⁰ According to the Montreal classification of IBD, UC can be categorized into the rectal type, left semicolon type, and extensive colon type.¹¹ Stages of UC can be divided into the active period and remission period. Using the modified Truelove and Witts severity index, the severity of the disease in the active period can be categorized into mild, moderate, or severe.¹² The modified Mayo score is used to evaluate the efficacy of clinical studies. Relief refers to the absence of clinical symptoms, with colonoscopy revealing a generally normal inflammatory response or the absence of an active inflammatory response. Effective treatment means that the clinical symptoms have essentially resolved, with only a mild mucosal inflammatory reaction found on colonoscopy. Ineffective treatment means that no mitigation of clinical symptoms or improvements observed on colonoscopy have been noted. UC relapse refers to the recurrence of UC symptoms following natural or drug treatment into the remission period. The most common symptoms of UC, namely bloody stool and diarrhea, can be confirmed through colonoscopy.

CD was classified according to the Montreal classification of IBD on the basis of age at diagnosis, the lesion site, and the disease behavior.¹¹ The CD Activity Index (CAI) was clinically used to assess the severity of disease activity and evaluate the efficacy of treatment, with CDAI of ≥ 150 corresponding to an active stage of disease. CDAI of < 150 was the criterion for clinical remission. Clinical remission of withdrawal hormones is defined as that occurring during the remission phase. A CDAI reduction of ≥ 100 points (or ≥ 70 points) is considered effective.¹³ Relapse refers to the reappearance of CD-related clinical symptoms and evidence of disease activity reflected by laboratory inflammatory response indicators and on endoscopy and imaging studies in the remission period following drug treatment.

Data collection

Relevant literature was searched to identify established risk factors for IBD recurrence. A self-report questionnaire was developed to obtain sociodemographic and lifestyle information, including data on dietary and drinking habits, assessments of the patient's condition, allergy history, and medical history. We centered our attention on long-term drinking, smoking, and dietary habits maintained prior to IBD diagnosis. Participants were asked about the number and size of portions of various food items that they consumed weekly. Attempts were made to establish whether the patients with IBD developed their condition due to their usual dietary habits. The validated FFQ surveyed the daily eating habits of patients with IBD 1 year before diagnosis and those of controls over the past year. To drive the recall of information on lifestyles over the previous year (e.g., information on eating habits), we included questions about family and social backgrounds. The questionnaire included items on 18 foods and drinks common to the Chinese diet. The questionnaires were distributed and collected by participating researchers or physicians under supervision, and unanswered questions were completed during interviews. Informed consent was obtained from each participant prior to their enrollment. The study protocol was approved by the Ethics Committee of Huadong Hospital.

Statistical methods

Analyses were conducted using IBM SPSS Statistics for Windows, version 22 (IBM Corp., Armonk, NY, USA). The clinical characteristics and 20 dietary factors of all the participants were statistically analyzed. Continuous variables are expressed as means \pm standard deviations. Under the assumption of a normal distribution, a two-sample independent t test was performed, and comparisons were conducted using the Student's t test. Qualitative data are presented with constituent ratios. Group comparisons by each factor were conducted using the χ^2 test, with the significance level set at $\alpha=0.05$. Univariate or multivariate analyses were performed to assess potential risk factors. Logistic regression analysis, with adjustments made for potential confounders, was conducted. Univariate analysis was performed for all variables in the multivariate analysis, and multivariate two-category conditional logistic regression analysis was undertaken for the significant variables. All analyses were two sided, and a *p* value of < 0.05 was considered significant.

Ethical considerations

All participants provided written informed consent. The Ethics Committee of Huadong Hospital approved the study protocol.

RESULTS

Association between IBD incidence and diet

We investigated possible dietary deficiencies in patients with IBD by comparing their dietary composition with those of controls. The generally nutritionally inadequate diets of patients with IBD, combined with related dietary problems such as food avoidance, can put these individuals at risk of malnutrition. Therefore, as a part of multidisciplinary care teams for IBD, registered dietitians

should conduct thorough nutritional assessment and provide patient education.

Clinical characteristics

Participants, comprising 50 patients with IBD (aged 52.0±14.4 years, 62% men) and 50 controls (aged 54.8±14.2 years, 64% men), were surveyed between October 1, 2016, and December 31, 2017 (Table 1). The age and sex distributions were comparable between cases and controls.

Food consumption and risk of IBD

To exclude the potential confounding effects of symptom-induced dietary changes, we only considered patients who did not change their dietary habits. As shown in Table 2, a single-factor analysis of the dietary components revealed significant between-group differences in the consumption of chili ($\chi^2=8.27$, $p=0.014$), fish ($\chi^2=12.3$, $p=0.02$), milk ($\chi^2=11.9$, $p=0.003$), nuts ($\chi^2=6.60$, $p=0.037$), eggs ($\chi^2=7.90$, $p=0.019$), and fruit ($\chi^2=26.5$, $p=0.001$).

These six factors were set as independent variables. According to the diet-related risk factor questionnaire, the independent variables were assigned the following values: 0 = do not consume at all or eat occasionally, 1 = consume 1-2 times per week, and 2 = consume ≥ 3 times per week. The incidence of IBD was set as the dependent variable (0 = no, 1 = yes), and multivariate logistic regression analysis was undertaken to examine the dietary factors potentially affecting IBD incidence. Moderate-to-high intake of fruit (1-2 times per week, OR = 0.225, 95% CI: 0.052–0.983, ≥ 3 times per week, OR = 0.053, 95% CI: 0.012–0.238) reduced the risk of IBD. The consumption of chili (≥ 3 times per week, OR = 3.38, 95% CI: 0.524–21.8), milk (≥ 3 times per week, OR = 3.39, 95% CI: 0.770–14.9), fish (1-2 times per week, OR = 5.73, 95% CI: 1.22–26.9), and nuts (1-2 times per week, OR = 4.83, 95% CI: 0.787–19.2) was positively correlated with IBD risk (Table 3). No significant correlations were noted for egg consumption.

IBD relapse and diet

By comparing research on IBD remission and relapse in patients with different clinical characteristics and dietary components, we determined high-risk dietary factors for IBD recurrence, as well as strategies for reducing malnutrition risk and remission maintenance.

Clinical characteristics

A total of 50 patients with IBD were included in this study. The 31 patients in the relapse group (mean baseline age: 53.2±12.2 years, 35% women) comprised 27 and 4 patients with UC and CD, respectively. The recurrence

rates of UC and CD were 67.5% and 40%, respectively. Among the 19 patients in the remission group (mean baseline age: 48.4±15.8 years, 42% women), 6 and 13 had CD and UC, respectively.

As presented in Table 4, no between-group differences were observed in age, sex ($p=0.64$), parenteral manifestations ($p=0.951$), complications ($p=0.619$), anemia ($p=0.589$), bloating ($p=0.951$), abdominal pain ($p=0.114$), or the Montreal classification (lesion range of UC: $p=0.785$, lesion range of CD: $p=0.367$, behavior: $p=0.213$, severity of CD lesions, $p=0.261$, upper gastrointestinal tract disease modifier: $p=0.157$). The two groups differed in disease phenotype ($p=0.019$), fever ($p=0.026$), blood ($p=0.007$), diarrhea ($p=0.013$), the Montreal classification (severity of UC lesions, $p=0.03$), and IBD medication use ($p=0.032$).

Multivariate logistic regression analysis demonstrated that blood was an independent risk factor for IBD recurrence (OR=4.50; 95% CI: 1.15–32.7, $p<0.05$). Although the differences in fever, diarrhea, and active IBD medication use were significant in the univariate analysis, they were not significant in the multivariate analysis (Table 5).

Dietary patterns

The consumption of fish ($\chi^2=3.90$, $p=0.048$), seafood ($\chi^2=5.12$, $p=0.024$), vegetables ($\chi^2=4.78$, $p=0.029$), nuts ($\chi^2=4.58$, $p=0.032$), beef ($\chi^2=5.53$, $p=0.019$), and fruit ($\chi^2=6.38$, $p=0.012$) between the recurrence and remission groups differed significantly, as did food allergy history ($\chi^2=5.52$, $p=0.019$; Table 6).

The logistic regression analysis indicated that the consumption of seafood (OR = 9.47; 95% CI: 1.40–14.0) and nuts (OR=9.02; 95% CI: 1.10–23.9) were risk factors for IBD recurrence, as was a history of food allergy (OR=7.75; 95% CI: 1.05–57.4). Differences in the consumption of fish, vegetables, beef, and fruit were significant in the univariate analysis but not in the multivariate analysis (Table 7).

DISCUSSION

The high recurrence rate is one of the most well-known clinical features of IBD. The recurrence rate of UC exceeds 50%.¹⁴ A population-based study reported a 5-year UC recurrence rate of 78.0% and indicated that patients with CD were prone to relapse, even following surgical intervention.¹⁵ In another investigation, the clinical recurrence rates of CD at 3 and 10 years after surgery were 30% and 60%, respectively, seriously undermining patients' quality of life.¹⁶ Herein, the recurrence rates of UC and CD were 67.5% and 40%, respectively. The evidence indicates that the incidence of IBD in China is increasing, and that the associated clinical problems are complex.

Table 1. Baseline patient characteristics

Characteristics	Cases (n=50)	Controls (n=50)	<i>p</i> value
Number	50	50	
Sex			
Males (%)	31 (62)	32 (64)	0.836
Females (%)	19 (38)	18 (36)	
Age (year)	52.0±14.4	54.8±14.2	0.659

Table 2. Food consumption and food allergy in the two groups

Food groups	Cases (n=50)	Controls (n=50)	χ^2	<i>p</i> value
Chili			8.27	0.014*
Not at all or occasionally	15	26		
1-2 times per week	21	20		
≥ 3 times per week	14	4		
Tea			2.07	0.335
Not at all or occasionally	28	30		
1-2 times per week	2	5		
≥ 3 times per week	20	15		
Alcohol			0.499	0.458
No	38	35		
Yes	12	15		
Fish			12.3	0.020*
Not at all or occasionally	14	28		
1-2 times per week	10	11		
≥ 3 times per week	26	11		
Milk			11.9	0.003*
Not at all or occasionally	26	30		
1-2 times per week	7	16		
≥ 3 times per week	17	4		
Seafood			5.88	0.053
Not at all or occasionally	22	30		
1-2 times per week	20	9		
≥ 3 times per week	8	11		
Sweets and cakes			2.01	0.366
Not at all or occasionally	14	20		
1-2 times per week	20	19		
≥ 3 times per week	16	11		
Fried food			5.48	0.064
Not at all or occasionally	23	30		
1-2 times per week	17	7		
≥ 3 times per week	10	13		
Carbonated drinks			0.383	0.862
Not at all or occasionally	27	24		
1-2 times per week	12	13		
≥ 3 times per week	11	13		
Vegetables			2.38	0.132
1-2 times per week	18	11		
≥ 3 times per week	32	39		
Nuts			6.60	0.033*
Not at all or occasionally	18	30		
1-2 times per week	20	15		
≥ 3 times per week	12	5		
Yogurt			5.01	0.082
Not at all or occasionally	26	15		
1-2 times per week	12	17		
≥ 3 times per week	12	18		
Coffee			1.18	0.554
Not at all or occasionally	23	19		
1-2 times per week	17	22		
≥ 3 times per week	7	9		
Diet structure			2.40	0.302
Meat-based	18	11		
Mix-based	21	25		
Vegetarian-based	11	14		
Eggs			7.90	0.019*
Not at all or occasionally	9	12		
1-2 times per week	18	6		
≥ 3 times per week	23	32		
Chicken			0.798	0.451
Not at all or occasionally	18	15		
1-2 times per week	20	21		
≥ 3 times per week	12	14		
Beef			1.47	0.480
Not at all or occasionally	27	21		
1-2 times per week	14	17		
≥ 3 times per week	9	12		

* $p < 0.05$

Table 2. Food consumption and food allergy in the two groups (cont.)

Food groups	Cases (n=50)	Controls (n=50)	χ^2	<i>p</i> value
Fruits			26.5	0.001*
Not at all or occasionally	32	9		
1-2 times per week	10	10		
≥ 3 times per week	8	31		
Pickles			2.27	0.322
Not at all or occasionally	28	32		
1-2 times per week	13	7		
≥ 3 times per week	9	11		
Food allergy			1.27	0.260
Yes	16	11		
No	34	39		

p*<0.05Table 3.** Multivariate logistic regression analysis of dietary factors related to IBD patients

	β value	SE	Wald	<i>p</i> value	OR	95% CI
Chili (0)			1.64	0.440		
Chili (1)	0.343	0.623	0.302	0.583	1.41	0.415–4.78
Chili (2)	1.22	0.951	1.64	0.020*	3.38	0.524–21.8
Milk (0)			2.64	0.267		
Milk (1)	0.351	0.689	0.259	0.611	1.42	0.368–5.48
Milk (2)	1.22	0.756	2.61	0.017*	3.39	0.770–14.9
Fish (0)			5.13	0.077		
Fish (1)	1.75	0.788	4.91	0.027*	5.73	1.22–26.9
Fish (2)	0.981	0.685	2.05	0.152	2.67	0.696–10.2
Nuts (0)			6.48	0.139		
Nuts (1)	1.58	0.645	5.96	0.015*	4.83	1.36–17.1
Nuts (2)	1.36	0.814	2.78	0.096	3.89	0.787–19.2
Eggs (0)			4.57	0.102		
Eggs (1)	1.15	0.777	2.20	0.138	3.16	0.690–14.5
Eggs (2)	1.76	0.826	4.55	0.053	5.82	1.15–29.4
Fruits (0)			14.7	0.051		
Fruits (1)	-1.49	0.751	3.93	0.047*	0.225	0.052–0.983
Fruits (2)	-2.94	0.765	14.7	0.000*	0.053	0.012–0.238

0: do not consume at all or eat occasionally; 1: consume 1-2 times per week; 2: consume ≥ 3 times per week.**p*<0.05.

Significant epidemiological and phenotypical differences between IBD in China and in the West include the lack of familial clustering,¹⁷ a milder clinical course, fewer extraintestinal manifestations and complications, and fewer fistulas and perianal complications.¹⁸ A meta-analysis examining the clinical data of 2283 patients with CD and 17,958 patients with UC in China found that the majority of patients with CD were diagnosed between 17 and 40 years of age, with non-stricturing and non-penetrating disease, varied lesion locations, and few extraintestinal manifestations. Patients with UC in China tend to be diagnosed at a later disease and with a more severe disease course, multisegmental lesions, and fewer extraintestinal manifestations.¹⁹ OCTN or CARD 15 gene variations are associated with susceptibility to IBD in Western populations. However, such variations are rare and may not be associated with susceptibility to IBD in Chinese patients.²⁰

Herein, the incidence of UC among patients with IBD was higher than that of CD; this is consistent with the fact that more patients with UC than patients with CD were enrolled. The small sample size may affect the results to a certain extent. We only considered patients who were diagnosed as having IBD within a year of the interview.

Differences in the foods examined and the grouping of patients complicate the comparison of our results with those of other studies. Certain fish species may have unknown elements that, when consumed on a regular basis, affect the activity and development of IBD. Given that our questionnaire cannot estimate the consumption of specific types of fish, such effects may have been overlooked. Furthermore, ascertaining whether the questionnaire data accurately reflect dietary information from 1 year prior to study commencement is challenging. Prospective studies are warranted to confirm the associations between diet and IBD risk. Our findings may serve as a reference for preventing IBD recurrence through the modification of patient diets in the remission period. However, considering the extremely low incidence of IBD, such studies are exceptionally difficult to perform. This is why we elected to conduct a case-control study. The supplemental interviews conducted by physicians to reduce the amount of missing data may have introduced some information bias given that the physicians possessed knowledge of their patients' conditions. The patients' recall of their diet from 1 year prior may have been influenced by their diet after the onset of disease, and some individuals may have received dietary education. In con-

Table 4. Comparison of IBD patients in the recurrence and remission groups

Characteristics	Flare (n=31)	Remission (n=19)	<i>p</i> value
Sex (female)	11 (35.5)	8 (42.1)	0.64
Age (years)	53.2±12.2	48.4±15.8	0.231
Disease phenotype			0.019*
UC	27 (67.5%)	13	
CD	4 (40%)	6	
Parenteral manifestations	26	11	0.951
Montreal classification			
UC			
E1: proctitis	6	5	0.785
E2: distal	16	8	
E3: extensive	3	2	
Mild	7	9	0.030*
Moderate	17	3	
severe	3	1	
CD			
L1: terminal ileum	2	4	0.367
L2: colon	2	1	
L3: ileocolon	0	1	
L4: upper gastrointestinal	1	0	0.157
B1: inflammatory	3	5	0.213
B2: stricturing	1	1	
B3: penetrating	0	0	
P: perianal	0	0	
Mild	2	5	0.261
Moderate	2	1	
Severe	0	0	
Medication			0.032*
5-ASA	17	12	
5-ASA + Systemic steroids	13	1	
5-ASA + Immunomodulators	1	0	
Complications	4	1	0.619
Anemia	9	2	0.589
Fever	16	2	0.026*
Blood	23	4	0.007*
Diarrhea	24	5	0.013*
Bloating	26	11	0.951
Abdominal pain	31	12	0.114

p*<0.05.Table 5.** Multivariate logistic regression analysis of clinical characteristics of the recurrence group

	β value	SE	Wald	<i>p</i> value	OR	95% CI
Fever	1.91	1.02	3.48	0.062	6.74	0.909~50.0
Diarrhea	1.60	0.911	3.07	0.08	4.94	0.828~29.5
Blood	1.81	0.854	4.50	0.034*	6.12	1.15~32.7
5-ASA			3.18	0.074		
5-ASA + Systemic steroids	1.41	2.22	0.403	0.526	4.10	0.053~18.7
5-ASA + Immunomodulators	3.29	2.37	1.92	0.166	26.8	0.256~27.6

**p*<0.05.

clusion, despite the small sample size, our study is one of the few studies providing information on the relevance between dietary habits and IBD, thus providing insights into the difficulties and uncertainties encountered in epidemiological studies on diet and IBD. Furthermore, this study revealed the contributions of environmental dietary factors to IBD risk and identified, through factor analysis, a specific dietary pattern predisposing individuals to IBD. The principal limitation of this investigation is recall bias, which is inevitable given its retrospective nature.

This case-control study found positive associations between the consumption of chili, milk, fish, and nuts and

IBD risk. Several risk factors for IBD in the Chinese population have been implicated in studies conducted in Mainland China.²¹⁻²² Based on the present results, a summary of relevant factors is presented in Table 8. A case-control study conducted at multiple Chinese medical centers concluded that the high consumption of sugary foods and meat increased CD incidence.²² Glucose is thought to inhibit intestinal absorption, and as the concentration of sugar in the intestinal lumen increases, microbial reproduction increases, resulting in increased intestinal permeability and inflammatory response.²³ The protective effect of smoking on UC is still unclear. It may be that some

Table 6. Food consumption and food allergy in the recurrence and remission groups

Food groups/Eat or Not Eat	Flare (n=31)	Remission (n=19)	χ^2	<i>p</i> value
Chili			0.101	0.75
Yes	6	3		
No	25	16		
Tea			0.002	0.96
Yes	10	6		
No	21	13		
Alcohol			0.001	0.975
Yes	5	3		
No	26	16		
Fish			3.90	0.048*
Yes	18	5		
No	15	14		
Milk			0.057	0.812
Yes	12	8		
No	19	11		
Seafood			5.12	0.024*
Yes	20	6		
No	11	13		
Sweets and cakes			0.085	0.771
Yes	16	9		
No	15	10		
Fried food			0.02	0.884
Yes	6	4		
No	25	15		
Carbonated drinks			0.002	0.968
Yes	8	5		
No	23	14		
Vegetables			4.78	0.029*
Yes	13	14		
No	18	5		
Nuts			4.58	0.032*
Yes	16	4		
No	15	15		
Yogurt			0.764	0.382
Yes	17	8		
No	14	11		
Coffee			0.193	0.660
Yes	5	4		
No	26	15		
Eggs			0.455	0.50
Yes	20	14		
No	11	5		
Chicken			0.141	0.707
Yes	18	10		
No	13	9		
Beef			5.53	0.019*
Yes	13	2		
No	18	17		
Diet structure			2.67	0.263
Vegetarian-based	10	10		
Mix-based	15	5		
Meat-based	6	4		
Fruits			6.38	0.012*
Yes	7	11		
No	24	8		
Pickles			0.082	0.775
Yes	4	3		
No	27	16		
Food allergy			5.52	0.019*
Yes	17	4		
No	14	15		

**p*<0.05.

Table 7. Multivariate logistic regression analysis of diet-related factors for IBD recurrence

	β value	SE	Wald	<i>p</i> value	OR	95% CI
Seafood	2.25	0.975	5.32	0.021*	9.47	1.40~14.0
Fish	0.816	0.915	0.796	0.372	2.26	0.376~13.6
Nuts	2.20	1.07	4.20	0.040*	9.02	1.10~23.9
Vegetables	-1.81	1.01	3.20	0.073	0.163	0.022~1.19
Beef	-0.752	1.08	0.485	0.486	0.471	0.057~3.92
Fruits	-1.48	1.10	1.80	0.179	0.228	0.026~1.97
Food allergy	2.05	1.02	4.02	0.045*	7.75	1.05~57.4

* *p*<0.05**Table 8.** Multivariate logistic regression analysis of diet-related factors for IBD recurrence

Factors	IBD	
	Risk	Protective
Heavy sugar consumption	+(22,28)	
Smoking		+(27)
Daily consumption of eggs	+(25)	
Often eating fried food	+(21, 26)	
History of allergy	+(21 [†])	
Milk	+(27 [†])	
Chili	+(28 [†])	

+ (reference numbers).

[†] Represents the current study.

components in tobacco can enhance the colonic mucosal barrier, reduce the synthesis of inflammatory mediators, and affect the immune system.²⁴ Several investigations have identified the high consumption of deep-fried food and spicy food, as well as the daily consumption of eggs and milk, as risk factors.²⁵⁻²⁸ During the preparation of fried food at high temperature, harmful substances, such as acrylamide contained in polycyclic aromatic hydrocarbons, can damage body DNA and induce colon cancer, and may cause IBD by reducing the local immune state of intestinal tract. Excessive fat or unsaturated fatty acids can form hypercholesterolemia, which makes blood in a hypercoagulable state, causes vasospasm, increases vascular tension, affects colonic mucosal blood supply and aggravates mucosal injury. Capsaicin is contained in chili peppers. High doses of capsaicin can cause excessive release of neurotransmitters in intestinal cells, resulting in long-term and irreversible damage to neurons sensitive to capsaicin, resulting in colon cell damage. Casein and bovine serum albumin in milk and other components, can act on gastrointestinal mucosa, cause gastrointestinal symptoms mainly allergic reactions. There were few studies on the relationship between allergy history and IBD. Some studies showed that allergy history is a high-risk factor for IBD, which is consistent with the results of our study. Traditional food allergies are mainly mediated by IgE, and most of them are type I and IV allergies with acute onset, while food intolerance is mostly IgG-mediated allergic diseases with insidious onset and delayed onset, and most of them are type II and III allergies with cumulative adverse reactions. Food is decomposed into amino acids, monosaccharides and glycerin, which can stimulate the body to produce specific IgG antibodies, forming immune complexes deposited in tissues and organs after combining with antigens, and causing immune damage. Several studies have focused on the role of dietary factors in IBD; some dietary factors have been con-

firmed to influence the development of IBD. Martini and Brandes (1976) reported the higher intake of refined carbohydrates in patients with CD than in controls.²⁹ Since then, several studies have evaluated other dietary factors relevant to patients with UC and CD, such as fiber, protein, and total calorie intake.^{8,30-35} One of these investigations (the study conducted by Reif et al) noted the correlation of the total protein intake and high egg consumption with IBD risk.⁸ The study also concluded that the high consumption of fruit, vegetables, and fiber helped protect against IBD risk. By contrast, two other studies did not find any differences between individuals with and without IBD.^{29,36} Epidemiological studies have demonstrated that the high consumption of total fat, omega-6 fatty acids, polyunsaturated fatty acids, and meat increases the risk of IBD development, whereas the high intake of fruits, fiber, and vegetables confers a protective effect.⁵ Given the numerous links between foods consumed, studies assessing the composition of individual diets are limited by potential confounders.³⁷

Various exclusion diets have been established in small case series and have been described as being effective for treating inflammation. Large-scale research is warranted to confirm these findings. These findings suggest that specific food components may promote inflammation. Complex interactions between food components in the food matrix and the gut microbiome may trigger and maintain the inflammatory cycle in IBD. The mechanism by which dietary intervention affects IBD inflammation remains unclear. Incipient research into the microbiome, proteome, and metabolome is expected to guide more targeted dietary therapies in the future. Dietary interventions, even simple shifts in fiber and fat consumption, lead to notable changes in the gut microbiome.³⁸⁻⁴⁰ Efforts have been devoted to developing therapies, including prebiotics, antibiotics, probiotics, and fecal microbiota transplantation, that selectively regulate the gut microbi-

ome. To ensure the continual formation of the microbiome, these therapies must be maintained in the long term.⁴¹ Dietary therapies that reshape food consumption patterns may alter exposure to harmful substances, such as selective food additives, that directly affect both the gut microbiome and the function of the host immune system.⁴² The mechanism of action of dietary therapy requires further exploration in clinical and preclinical models.

As with drugs, diets are not effective for all patients. Personalized diets may help resolve this problem. They can be implemented both as a monotherapy and in conjunction with immunosuppressants. Patients typically change their diets not only for symptom relief but also for inflammation control.⁴³ The implementation of dietary changes is usually guided by individual studies and anecdotal experience, and for most patients with IBD, such alterations are not included as a part of their treatment plan under the guidance of their medical team.⁴⁴ Research efforts on and the use of dietary interventions are mainly driven by patients themselves; many medical practitioners remain skeptical of and know little about dietary interventions. The compliance of patients with IBD and their families with stringent dietary requirements indicate that such diets confer tangible benefits. Because long-term dietary changes are required, family support and community support are critical to the success of patients' adherence to treatment. Medical teams should have patients discuss their eating patterns and understand the basics of common IBD exclusion diets. Furthermore, clinicians should work closely with patients to monitor their nutritional status and disease activity.

Despite the various challenges of using dietary therapies to treat IBD, patients urgently seek and follow such interventions. Many people change their eating habits based on different sources of information, as well in response to the onset of IBD symptoms. The effectiveness of dietary recommendations is variable, and comprehensive data are required to clarify the role of diet in active IBD. Food-based IBD trials typically involve elimination, supplementation, or considerable changes in dietary patterns.³⁷ The desire to avoid or reduce the degree of immunosuppression or to supplement existing drug therapy is a common driving factor. Given the costs associated with dietary adjustments, time spent on food preparation, and dietary restrictions, nutritional therapy may not be an attractive option for many patients; all patients and families do not have equal interest in dietary therapies. Dietary trials present challenges, but dietary interventions represent a unique opportunity to treat disease. The association of dietary exposure with IBD risk is widely established, but diet as a treatment has not been fully integrated into the broader IBD treatment paradigm. Considering that diet is a fundamental aspect of daily life and has infinite variation, it is a potential target for deeper intervention.

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AUTHOR DISCLOSURES

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