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Is fasting beneficial for hospitalized patients with inflammatory bowel diseases?

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Background/Aims: Patients with inflammatory bowel disease (IBD) are usually hospitalized because of aggravated gastrointestinal symptoms. Many clinicians empirically advise these patients to fast once they are admitted. However, there has been no evidence that maintaining a complete bowel rest improves the disease course. Therefore, we aimed to investigate the effects of fasting on disease course in admitted patients with IBD or intestinal Behçet's disease. **Methods:** A total of 222 patients with IBD or intestinal Behçet's disease, who were admitted for disease-related symptoms, were retrospectively analyzed. We divided them into 2 groups: fasting group (allowed to take sips of water but no food at the time of admission) and dietary group (received liquid, soft, or general diet). **Results:** On admission, 124 patients (55.9%) started fasting and 98 patients (44.1%) started diet immediately. Among patients hospitalized through the emergency room, a significantly higher proportion underwent fasting (63.7% vs. 21.4%, $P<0.001$); however, 96.0% of the patients experienced dietary changes. Corticosteroid use ($P<0.001$; hazard ratio, 2.445; 95% confidence interval, 1.506–3.969) was significantly associated with a reduction in the disease activity score, although there was no significant difference between the fasting group and the dietary group in disease activity reduction ($P=0.111$) on multivariate analysis. **Conclusions:** In terms of disease activity reduction, there was no significant difference between the fasting and dietary groups in admitted patients with IBD, suggesting that imprudent fasting is not helpful in improving the disease course. Therefore, peroral diet should not be avoided unless not tolerated by the patient. **(Intest Res 2020;18:85-95)**

Key Words: Fasting; Inflammatory bowel disease; Intestinal Behçet's disease; Colitis, ulcerative; Crohn disease

INTRODUCTION

Inflammatory bowel diseases (IBDs) including UC and CD are chronic inflammatory GI disorders of unknown etiology that are characterized by recurrent GI symptoms such as diarrhea, bleeding, and abdominal pain.[1] Patients with IBD present with varying clinical symptoms and various clinical courses, ranging from quiescent to acute or chronic refractory disease, often leading to repetitive hospitalizations because of disease exacerbation.[2,3] In addition, intestinal Behçet's disease (BD), a chronic, relapsing, inflammatory disorder, presents with a variety of bowel symptoms similar to those of IBD, including GI bleeding and abdominal pain.[4,5] Therefore, the treatment approaches for intestinal BD are usually comparable to those for IBD. Traditionally, when patients with IBD or intestinal BD are hospitalized because of acute exacerbation, fasting is frequently recommended for the purpose of resting the bowel, regardless of the disease site or the individual patient's condition.

Fasting can reduce inflammation by decreasing the number of luminal bacteria and antigens in the colon and can affect

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the anabolic pathway, thus altering the immune system and inflammation.[6] However, the role of fasting in patients with IBD is still not fully understood. Some studies have reported that fasting with administration of total parenteral nutrition (TPN) has positive effects on nutritional deficits and as perioperative nutritional support.[7,8] Particularly in patients with CD, TPN with bowel rest is recommended for the following indications: impossible enteral nutrition (EN), avoidance of EN for medical reasons, signs or symptoms of ileus or subileus in the small intestine, and presence of intestinal fistulae.[9] In addition, Müller et al.[10] reported that after administering TPN for 3 weeks with an additional 9-week course administered at home, surgery could be avoided in 25 of 30 patients with CD. However, several preliminary studies recently reported that EN is more effective than complete bowel rest through fasting in patients with severe IBD.[11-14]

There is a lack of studies showing how often fasting is being recommended for patients with IBD or intestinal BD and whether there is a difference in the diet prescription according to disease activity. Furthermore, it is still debatable whether fasting is helpful in patients with IBD. Therefore, we aimed to investigate the effects of fasting in admitted patients with IBD or intestinal BD. Moreover, we investigated how frequently fasting is actually prescribed and which patients are mainly prescribed to fast.

METHODS

1. Patients

Between March 2016 and February 2017, we retrospectively reviewed 246 hospitalized patients with IBD or intestinal BD at Severance Hospital, Yonsei University College of Medicine, Seoul, Korea. The diagnosis of UC and CD was based on clinical, endoscopic, histopathologic, and radiologic findings[15,16] and the diagnosis of intestinal BD was made as previously established (based on clinical manifestations and colonoscopic findings).[17] A total of 222 patients were finally enrolled into the study. Twenty-four patients were excluded for meeting the following exclusion criteria: (1) suspected appearance of any other GI diseases such as nonspecific colitis, intestinal tuberculosis, or ischemic colitis during the follow-up period; (2) age <18 years; (3) no available clinical data such as disease activity or clinical records; and (4) could not be followed up during the study period.

We divided the patients into 2 groups according to the diet prescription pattern. The fasting group included patients who received prescriptions of nil per os (NPO, no oral intake including water) or sips of water (SOW, water intake only) at the time of admission. The dietary group included patients who were prescribed liquid diet (including clear liquid diet [CLD, such as water, broth, and plain gelatin] and full liquid diet [FLD, consisting of both clear and opaque liquid foods with a smooth consistency]), soft diet (foods that are physically soft, such as porridge), or general diet. Finally, 124 patients were included in the fasting group and 98 patients were included in the dietary group. As a retrospective study, the informed consent was waived. This study was performed in accordance with the ethical guidelines of the 1975 Declaration of Helsinki and approved by the Institutional Review Board of Severance Hospital (IRB No. 2019-0453-001).

2. Assessment of Nutrition Status

To assess the nutritional status of hospitalized patients, the Severance Nutrition Screening Index[18] was used. It includes changes in food intake, weight loss, BMI and serum albumin level, and is classified into low-risk and high-risk of malnutrition conditions using a cutoff score of 13.5.

3. Baseline Patient Characteristics

The baseline characteristics of the patients were obtained from electronic medical data collected during hospitalizations, including patient demographics, comorbid diseases, medication records at admission, types of nutrition route (e.g., TPN, EN, or oral nutrition) at hospitalization, previous bowel operation, and process of admission (e.g., through the emergency room [ER] or outpatient clinic). EN is a method of administering a nutritional formulation (Encover®: JW Choongwae pharm, Seoul, Korea or Harmonilan®: Yungjin Pharm, Seoul, Korea) through a Levin tube, gastrostomy, or jejunostomy, bypassing the oral cavity and supplying nutrients directly to the GI tract.[19]

To evaluate the effects of fasting in hospitalized patients with IBD or intestinal BD, we investigated disease activity, laboratory findings such as ESR and CRP levels, and readmission rates.

4. Assessment of Disease Activity

The disease activity of UC was assessed using the Mayo score and partial Mayo score. The Mayo score was calculated according to the following 4 factors: (1) bowel frequency, (2) rectal bleeding, (3) endoscopic findings, and (4) physician assessment. Partial Mayo score was calculated in the same manner but excluding the endoscopic score.[20,21] CD disease activity was assessed using CDAI.[22] To evaluate the disease activity of

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intestinal BD, we used the disease activity index of intestinal BD (DAIBD) based on 8 variables including general well-being, fever, extraintestinal manifestations, abdominal pain, abdominal mass, tenderness, intestinal complications, and number of liquid stools. The higher the score, the higher the disease activity.[23]

To analyze the change in disease activity, we calculated the disease activity score at the time of admission and after 1 week. We defined disease activity reduction as having a clinical response after 1 week from admission or before discharge. In patients with UC, clinical response was defined as a decrease from baseline of ≥30% and ≥3 points in the Mayo score, along with either a rectal bleeding subscore of 0 or 1 or a decrease from baseline of ≥1 in the rectal bleeding subscore, or a reduction by ≥2 points and 25% in the partial Mayo score compared to baseline.[24] In patients with CD, the response to treatment was defined as a reduction in CDAI of ≥70–100.[25] In patients with intestinal BD, clinical response was defined as a decrease in the DAIBD score of ≥20 points from the baseline value.[26]

5. Statistical Analysis

Variables were expressed as median (interquartile range [IQR]) or number (%). The baseline characteristics were compared using independent Student *t*-test (or Mann-Whitney test) for continuous variables and the chi-square test (or Fisher exact test) for categorical variables, as appropriate. We compared whether dietary prescriptions were associated with reduced disease activity and readmission. The independent predictors of reduction in disease activity, ESR, and CRP levels were analyzed using Cox regression analysis. Hazard ratios (HRs) and the corresponding 95% CIs were calculated. In addition, factors related to readmission within 3 months were analyzed using logistic regression analysis. ORs and the corresponding 95% CIs were calculated. The overall cumulative risk rates of disease activity reduction were analyzed using the Kaplan-Meier method and compared using the log-rank test. Data were analyzed using SPSS software version 25.0 (IBM Corp., Armonk, NY, USA). A *P*-value of <0.05 was considered statistically significant.

RESULTS

1. Baseline Characteristics of the Fasting and Dietary Groups at Hospitalization

The baseline characteristics of the fasting group (NPO or SOW) and the dietary group (CLD, FLD, soft diet, and general diet) are summarized in Table 1. A total of 222 patients with IBD or intestinal BD were hospitalized for disease aggravation between March 2016 and February 2017. Among them, 75 patients had UC (33.8%), 82 patients had CD (36.9%), and 65 patients had intestinal BD (29.3%). The median age at admission was 40 years (IQR, 27–51 years), and 48.2% of the patients were men. There was no significant difference between the fasting and dietary groups in sex and age. The median admission duration was 9 days (IQR, 5–15 days). There was no difference in whether the patients were hospitalized through the ER (45.0%) or the outpatient clinic (55.0%) at the time of admission; however, hospitalization through the ER was significantly more frequent in the fasting group (63.7% vs. 21.4%, $P<0.001$). The most common reason for admission was abdominal pain (39.2%), followed by general weakness (13.1%), GI bleeding (11.7%), disease work-up (9.5%), diarrhea (7.7%), and fever (7.2%). More patients in the fasting group were hospitalized because of abdominal pain (43.5% vs. 33.7%) or GI bleeding (15.3% vs. 7.1%) than those in the dietary group. In patients in the dietary group, the most common reason for admission was abdominal pain, but they were often hospitalized because of other GI symptoms such as nausea and vomiting, or for changing of medications or disease reassessment. There was a difference in the main symptoms between the 2 groups ($P=0.029$) (Table 1).

Patients in the fasting group more frequently changed their diet prescriptions during the hospital stay than did those in the dietary group (96.0% vs. 32.7%, $P<0.001$). The most frequent dietary prescription among the fasting group of patients with dietary changes was soft diet (29.4%), followed by CLD (27.7%), FLD (16.0%), SOW (13.4%), and general diet (11.8%). In addition, a considerable number of the dietary group patients simultaneously received TPN (79.6%) or additional EN such as Encover® or Harmonilan® (10.2%). However, there was no significant difference in BMI, underlying diseases, medications, and history of bowel operation between the fasting and dietary groups (Table 1).

2. Outcomes

We evaluated the laboratory findings including hemoglobin, ESR, and CRP levels to estimate disease activity and nutritional status. Laboratory tests were performed at the time of hospital admission and at 1 week after admission and/or before discharge. There were no significant changes in the baseline and follow-up laboratory findings between the 2 groups (all

Table 1. Baseline Characteristics of the Fasting Group and the Dietary Group at Hospitalization

Variable	Total (n = 222)	Fasting group (n = 124)[a]	Dietary group (n = 98)[b]	*P*-value[c]
Male sex	107 (48.2)	60 (48.4)	47 (48.0)	0.949
Age at admission (yr)	40 (27–51)	39 (25–49)	40 (31–52)	0.296
Admission days	9 (5–15)	9 (5–15)	8 (5–14)	0.901
Process of admission				
Emergency room	100 (45.0)	79 (63.7)	21 (21.4)	< 0.001
Outpatient clinic	122 (55.0)	45 (36.3)	77 (78.6)	< 0.001
Reasons for admission				0.029
Abdominal pain	87 (39.2)	54 (43.5)	33 (33.7)	
GI bleeding	26 (11.7)	19 (15.3)	7 (7.1)	
Fever	16 (7.2)	7 (5.6)	9 (9.2)	
Diarrhea	17 (7.7)	11 (8.9)	6 (6.1)	
Screening or work-up	21 (9.5)	9 (7.3)	12 (12.2)	
General weakness	29 (13.1)	16 (12.9)	13 (13.3)	
Others[d]	26 (11.7)	8 (6.5)	18 (18.4)	
Body weight (kg)	55.0 (48.0–61.0)	55.0 (50.3–62.0)	52.0 (47.0–60.0)	0.685
BMI (kg/m^2)	20.1 (18.0–22.5)	20.3 (18.3–22.5)	19.8 (17.6–22.1)	0.290
Type of IBD				0.242
UC	75 (33.8)	36 (29.0)	39 (39.8)	
CD	82 (36.9)	49 (39.5)	33 (33.7)	
Intestinal Behçet's disease	65 (29.3)	39 (31.5)	26 (26.5)	
Consultation with the nutritional team	65 (29.3)	39 (31.5)	26 (26.5)	0.424
Nutritional status by SNSI				0.709
Low risk of malnutrition	158 (71.2)	87 (70.2)	71 (72.4)	
High risk of malnutrition	64 (28.8)	37 (29.8)	27 (27.6)	
Change in diet prescription	151 (68.0)	119 (96.0)	32 (32.7)	< 0.001
Medications				
5-ASA	195 (87.8)	111 (89.5)	84 (85.7)	0.389
Steroids	108 (48.6)	58 (46.8)	50 (51.0)	0.530
Immunomodulators	89 (40.1)	48 (38.7)	41 (41.8)	0.637
Methotrexate	18 (8.1)	8 (6.5)	10 (10.2)	0.309
Anti-TNF agents	48 (21.6)	21 (16.9)	27 (27.6)	0.056
Total parenteral nutrition	191 (86.0)	113 (91.1)	78 (79.6)	0.014
Enteral nutrition	29 (13.1)	19 (15.3)	10 (10.2)	0.261
Previous bowel operation	97 (43.7)	56 (45.2)	41 (41.8)	0.620
Underlying disease				
Hypertension	19 (8.6)	11 (8.9)	8 (8.2)	0.852
Diabetes	11 (5.0)	5 (4.0)	6 (6.1)	0.476
Tuberculosis	25 (11.3)	13 (10.5)	12 (12.2)	0.680
Hematologic disorder	37 (16.7)	16 (12.9)	21 (21.4)	0.091

Values are presented as number (%) or median (interquartile range).
[a]Fasting group: no oral intake including water or water intake only.
[b]Dietary group: liquid, soft, general diet.
[c]*P*-value for comparing patients with fasting group and dietary group.
[d]Others: nausea, vomiting, medication change, perianal abscess, etc.
SNSI, Severance Nutrition Screening Index; 5-ASA, 5-aminosalicylic acid.

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$P>0.05$). Further, our study population did not show any differences in baseline disease activity between the fasting and dietary groups (all $P>0.05$) (Table 2). There was no significant difference in the follow-up scores of disease activity in each disease group, such as UC (partial Mayo score, $P=0.953$ and Mayo score, $P=0.155$), CD ($P=0.248$), and intestinal BD ($P=0.239$), and in the proportion of patients with a reduction in disease activity score between with and without fasting (fasting group 66.1% vs. dietary group 68.4%, $P=0.724$). Finally, the readmission rate within 3 months after discharge also did not show a significant difference between the fasting and dietary groups (56.5% vs. 54.1%, $P=0.724$).

3. Risk Factors Related to Disease Activity and Readmission

In the univariate analysis of Cox regression models, corticosteroid use (HR, 2.116; 95% CI, 1.507–2.970; $P<0.001$) was found to be a significant factor in reducing disease activity. Variables including male sex, admission through the ER, CD and intestinal BD compared with UC, high initial hemoglobin, and albumin levels were negatively associated with reduced disease activity score (all $P<0.05$) (Table 3). In the multivariate analysis with adjustment for age at admission, medications, body weight, albumin, ESR, and CRP levels, corticosteroid use (adjusted HR, 2.445; 95% CI, 1.506–3.969; $P<0.001$) was found to be the only significant factor in reducing disease activity, and male sex (adjusted HR, 0.661; 95% CI, 0.441–0.990; $P=0.044$),

Table 2. Outcomes of the Fasting and Dietary Groups

Variable	Total (n = 222)	Fasting group (n = 124)[a]	Dietary group (n = 98)[b]	*P*-value[c]
Laboratory findings				
Hemoglobin (g/dL)	11.6 (10.0–13.6)	12.0 (10.0–14.0)	11.1 (10.0–13.0)	0.174
Initial ESR (mm/hr)	50.5 (26.0–83.8)	48.0 (22.0–84.5)	52.0 (33.0–83.0)	0.525
Follow-up ESR (mm/hr)	33.0 (15.3–59.0)	10.0 (7.0–23.0)	36.0 (17.5–58.5)	0.562
Initial CRP (mg/L)	30.5 (5.7–103.7)	23.5 (3.8–104.9)	33.6 (9.0–103.9)	0.754
Follow-up CRP (mg/L)	6.3 (1.4–23.4)	6.4 (1.2–22.9)	6.1 (1.7–25.8)	0.296
Initial albumin (g/dL)	3.6 (3.0–4.0)	3.6 (3.0–4.0)	3.6 (3.0–4.0)	0.908
Follow-up albumin (g/dL)	3.4 (2.8–4.0)	3.5 (2.9–4.0)	3.2 (2.5–3.9)	0.002
Disease activity				
UC				
Partial Mayo score	6.0 (4.0–7.0)	5.5 (4.0–8.3)	6.0 (3.5–7.0)	0.685
Mayo score	11.0 (8.0–13.0)	11.5 (9.8–14.3)	10.0 (7.0–12.3)	0.064
CD	322.0 (236.0–425.0)	308.0 (227.5–399.5)	353.0 (281.5–461.0)	0.065
Intestinal Behçet's disease	90.0 (50.0–130.0)	80.0 (50.0–120.0)	80.0 (50.0–120.0)	0.690
Follow-up disease activity				
UC				
Partial Mayo score	3.0 (2.0–5.0)	3.0 (2.0–5.0)	3.0 (2.0–5.5)	0.953
Mayo score	6.0 (4.0–7.8)	6.0 (4.3–8.0)	4.5 (3.0–6.8)	0.155
CD	320.5 (257.0–375.3)	319.0 (286.5–393.5)	322.0 (236.0–365.5)	0.248
Intestinal Behçet's disease	50.0 (25.0–80.0)	55.0 (27.5–105.0)	40.0 (20.0–60.0)	0.239
DAI reduction	149 (67.1)	82 (66.1)	67 (68.4)	0.724
Readmission	123 (55.4)	70 (56.5)	53 (54.1)	0.724

Values are presented as median (interquartile range) or number (%).
[a]Fasting group: no oral intake including water or water intake only.
[b]Dietary group: liquid, soft, general diet.
[c]*P*-value for comparing patients with fasting group and dietary group.
DAI, disease activity index.

Table 3. Factors Involved in Reducing the Disease Activity Score (Cox Regression Analysis)

Variable	Univariate analysis		Multivariate analysis	
	P-value	HR (95% CI)	*P*-value	Adjusted HR (95% CI)
Male sex	0.024	0.681 (0.488–0.950)	0.044	0.661 (0.441–0.990)
Age at admission (yr)	0.595	1.003 (0.992–1.014)	0.200	0.990 (0.975–1.005)
Hospital stay (day)	0.838	1.001 (0.989–1.014)		
Diet prescription				
Dietary group		1 (reference)		1 (reference)
Fasting group	0.825	0.964 (0.697–1.334)	0.111	1.376 (0.929–2.039)
Body weight (kg) at admission	0.078	0.985 (0.968–1.002)	0.604	0.994 (0.974–1.016)
BMI (kg/m^2)	0.917	0.997 (0.949–1.048)		
Process of admission				
Outpatient clinic		1 (reference)		1 (reference)
Emergency room	0.025	0.684 (0.491–0.954)	0.023	0.638 (0.434–0.939)
Type of IBD				
UC		1 (reference)		1 (reference)
CD	<0.001	0.432 (0.290–0.644)	0.067	0.574 (0.317–1.040)
Intestinal Behçet's disease	0.001	0.498 (0.331–0.748)	0.001	0.397 (0.233–0.676)
Underlying disease				
Hypertension	0.845	1.061 (0.587–1.917)		
Diabetes	0.746	0.889 (0.435–1.816)		
Hematologic disorder	0.774	0.936 (0.593–1.475)		
Laboratory findings				
Hemoglobin (g/dL)	0.004	0.908 (0.851–0.969)	0.045	0.906 (0.824–0.998)
Albumin (g/dL)	0.009	0.739 (0.589–0.927)	0.594	0.912 (0.652–1.277)
ESR (mm/hr)	0.363	1.002 (0.997–1.008)	0.452	1.003 (0.995–1.011)
CRP (mg/L)	0.392	0.999 (0.997–1.001)	0.148	0.998 (0.995–1.001)
Medications				
5-ASA	0.185	1.451 (0.836–2.518)	0.151	1.597 (0.843–3.025)
Corticosteroids	<0.001	2.116 (1.507–2.970)	<0.001	2.445 (1.506–3.969)
Immunomodulators	0.219	0.811 (0.581–1.132)	0.861	0.964 (0.637–1.459)
Anti-TNF agents	0.590	0.893 (0.590–1.350)	0.263	0.745 (0.445–1.247)
Others[a]	0.437	1.230 (0.730–2.072)	0.554	1.229 (0.621–2.430)
Nutritional support			-	-
TPN	0.422	0.833 (0.533–1.302)		
EN	0.719	0.915 (0.564–1.485)		

[a]Others: methotrexate, 6-mercaptopurine.
5-ASA, 5-aminosalicylic acid; TPN, total parenteral nutrition; EN, enteral nutrition.

admission through the ER (adjusted HR, 0.638; 95% CI, 0.434–0.939; *P*=0.023), intestinal BD (adjusted HR, 0.397; 95% CI, 0.233–0.676; *P*=0.001) compared with UC, and high initial hemoglobin level (adjusted HR, 0.906; 95% CI, 0.824–0.998; *P*=0.045) were negative factors. Importantly, the fasting group did not show any significant superiority in reducing disease activity compared with the dietary group (adjusted HR, 1.376; 95% CI, 0.929–2.039; *P*=0.111) (Table 3). Furthermore, there was no significant difference in disease activity reduction between the fasting and dietary groups in the log-rank curve

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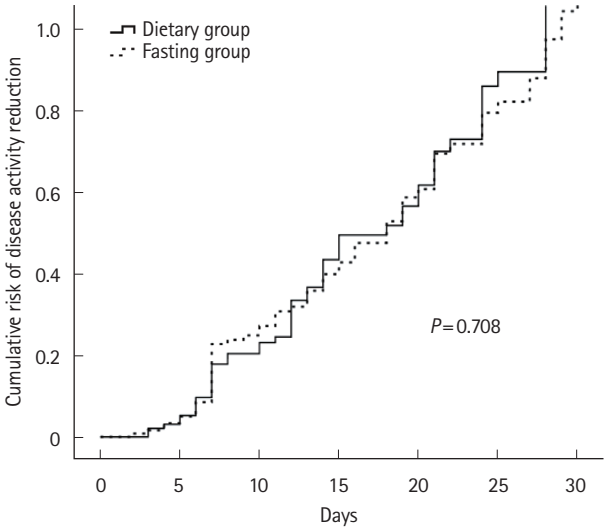

Fig. 1. Cumulative risk of disease activity reduction between the different diet prescriptions: dietary group and fasting group (Kaplan-Meier curves). Dietary group: liquid, soft, general diet; fasting group: no oral intake including water or water intake only.

(P=0.708) (Fig. 1).

In addition, we performed a subgroup analysis except for patients with abdominal pain and GI hemorrhage (n=109), because it was thought that therapeutic fasting was required for these patients regardless of disease activity. There was no significant difference in the reduction of disease activity in the fasting group (adjusted HR, 1.730; 95% CI, 0.955–3.134; P=0.071) when patients with abdominal and GI bleeding were excluded at admission compared with diet group. In multivariate analysis, intestinal BD (adjusted HR, 0.353; 95% CI, 0.167–0.745; P=0.006) compared with UC was a negative factor, while corticosteroids (adjusted HR, 4.757; 95% CI, 2.149–10.526; P<0.001) was an important factor in reducing disease activity in hospitalized IBD patients (data not shown). Moreover, when we analyzed the predictive factors of CRP level change, the factors associated with decreased CRP levels were age at admission, albumin, and other medications on multivariate analysis (P<0.05) (Supplementary Table 1).

The median days to readmission were 61 days (IQR, 21–131 days). In the logistic multivariate analysis, intestinal BD (adjusted OR, 3.263; 95% CI, 1.303–8.171; P=0.012) compared with UC was a significantly different factor related to readmission. In addition, high initial hemoglobin level (adjusted OR, 0.841; 95% CI, 0.711–0.995; P=0.044) was negatively associated with early readmission. However, the fasting group did not show a significant difference in readmission compared with the dietary group (Table 4).

DISCUSSION

Although the importance of nutrition and diet is well known in patients with IBD,[27,28] it remains controversial whether prescribing fasting is helpful in patients hospitalized because of symptom exacerbation. Our study shows that fasting is not effective in decreasing the disease activity and readmission rate in patients with IBD or intestinal BD. In addition, we noticed that in cases of hospitalization through the ER (n=79, 63.7%) and in patients with abdominal pain (n=54, 43.5%) or bleeding (n=19, 15.3%) at admission, the rate of fasting prescription was high.

In patients with IBD, diet is associated with disease pathogenesis, flare-up, and treatment.[28-30] Several studies have reported that diet plays a role in altering the immune system together with the intestinal microbiota in patients with IBD.[31-34] In an etiologic point of view, it is known that Western diets, which consist of refined grains, alcohol, salt, oil, meat, fats, polyunsaturated fatty acids, omega-6 fatty acids, and fructose, and are low in vegetables and fruits, can be considered environmental factors promoting inflammation in genetically susceptible hosts.[35,36] In addition, Jowett et al.[37] reported that higher consumption of meat, eggs, protein, and alcohol is related the relapse of UC. Several studies have reported the role of FODMAP (fermentable oligosaccharides, disaccharides and monosaccharides, and polyols), which could increase GI symptoms such as diarrhea, abdominal pain, and bloating in patients with IBD.[38,39] Dietary treatment is often used, such as exclusive and partial EN, specific carbohydrate diet, or gluten-free diet. Exclusive EN is effective, and according to the European Society for Clinical Nutrition and Metabolism (ESPEN) guideline, it is recommended as the first-line therapy to induce remission in children and adolescents with acute active CD.[40] However, there is no evidence on the therapeutic benefits of an elimination diet and TPN in patients with UC,[11] and the use of these dietary interventions in adult patients with CD is controversial.[41,42] Especially in patients with active IBD, there is no "IBD diet" to promote remission in the ESPEN guideline.[40]

Although there is no standardized specific IBD diet, several guidelines recommend a normal diet or EN, unless the diet is not tolerated, in patients with active UC.[43,44] Further, a positive effect of EN has been reported in patients with active CD.[40,45] Dickinson et al.[46] reported a controlled trial of intravenous hyperalimentation and total bowel rest for the treatment of acute colitis in 38 patients including 27 patients with UC and 9 patients with CD, and showed that intravenous hyperalimenta-

Table 4. Factors Involved in Readmission within 3 Months

Variable	Univariate analysis		Multivariate analysis	
	P-value	OR (95% CI)	*P*-value	Adjusted OR (95% CI)
Male sex	0.160	0.674 (0.388-1.169)	0.554	1.249 (0.597-2.612)
Age at admission (yr)	0.002	1.029 (1.010-1.049)	0.119	1.021 (0.995-1.048)
Hospital stay (day)	0.211	1.015 (0.992-1.039)		
Diet prescription				
Dietary group		1 (reference)		1 (reference)
Fasting group	0.946	0.981 (0.566-1.701)	0.620	1.201 (0.583-2.475)
Body weight (kg) at admission	0.007	0.960 (0.931-0.989)	0.163	0.972 (0.934-1.012)
BMI (kg/m^2)	0.306	0.955 (0.874-1.043)		
Process of admission				
Out-patients clinic		1 (reference)		1 (reference)
Emergency room	0.677	0.890 (0.513-1.543)	0.598	0.823 (0.398-1.699)
Type of IBD				
UC		1 (reference)		1 (reference)
CD	0.727	0.883 (0.440-1.773)	0.627	0.771 (0.270-2.203)
Intestinal Behçet's disease	0.001	3.183 (1.583-6.402)	0.012	3.263 (1.303-8.171)
Lab findings				
Hemoglobin (g/dL)	<0.001	0.784 (0.694-0.886)	0.044	0.841 (0.711-0.995)
Albumin (g/dL)	0.007	0.576 (0.385-0.863)	0.864	1.056 (0.564-1.980)
ESR (mm/hr)	0.020	1.010 (1.002-1.019)	0.705	1.002 (0.990-1.015)
CRP (mg/L)	0.018	1.004 (1.001-1.007)	0.769	0.999 (0.995-1.004)
Medications				
5-ASA	0.949	0.973 (0.423-2.241)	0.431	1.534 (0.529-4.447)
Corticosteroids	0.469	1.224 (0.708-2.115)	0.233	0.626 (0.290-1.352)
Immunomodulators	0.035	0.537 (0.302-0.956)	0.700	0.863 (0.409-1.822)
Anti-TNF agents	0.239	1.478 (0.771-2.832)	0.345	1.520 (0.637-3.627)
Others[a]	0.170	1.857 (0.767-4.499)	0.468	1.618 (0.441-5.937)
Nutritional support			-	-
TPN	0.782	0.895 (0.410-1.955)		
EN	0.558	1.269 (0.573-2.810)		

[a]Others: methotrexate, 6-mercaptopurine.
5-ASA, 5-aminosalicylic acid; TPN, total parenteral nutrition; EN, enteral nutrition.

tion and bowel rest had no therapeutic effect in acute colitis. According to the second Korean guideline and Toronto consensus statements, normal diet or EN is recommended for patients with UC except for certain extreme cases in which it is not possible.[43,44] Our study also showed that despite the high prescription rates of fasting at the time of hospitalization and fasting with TPN in hospitalized patients with IBD, there was no additional benefit in the fasting group compared with the dietary group. In addition, there was also no significant relationship between fasting and disease activity according to each disease (UC, CD, and intestinal BD).

In patients with IBD, readmission is an important factor affecting the quality of life, disease burden, and cost of hospitalization. Therefore, many studies have investigated the factors related to readmission in patients with IBD, such as chronic abdominal pain, infection, steroid use, and depression.[47,48] However, our study showed that fasting at admission was not associated with a reduction in the readmission rate.

To our knowledge, this is the first study to include both patients with IBD and patients with intestinal BD, and to show that dietary status is not related to disease activity and readmission. However, our study has several limitations. First, as this was a retrospective cohort study based on the clinical records, and performed in a single tertiary medical center, a selection bias and unmeasured confounding factors may exist. However, our medical center is large and has an IBD clinic that attends to many patients with IBD or intestinal BD. In addition, we did not use early EN or partial EN protocols, as these are used in pediatric patients. Further, our analysis was limited to short-term outcomes because only 1-year inpatient data were analyzed. Second, because our analysis was based on the diet prescription at the time of admission, it includes a shorter fasting time than the fasting period required to rest the bowel. However, it can be said our analyzed prescriptions were very similar to those used in clinical practice. Therefore, further well-designed studies with a large population are needed in the future.

In summary, there was no significant difference between the fasting and dietary groups in terms of reduction of disease activity in hospitalized patients with IBD or intestinal BD. Imprudent fasting prescriptions do not help in reducing the disease activity and readmission rate. Therefore, diet should not be avoided in patients with IBD unless it is not tolerated.

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CONFLICT OF INTEREST

Cheon JH has been the Editor of *Intestinal Research* since 2013. However, he was not involved in the peer reviewer selection, evaluation, or decision of this article. No other potential conflict of interest relevant to this article was reported.

AUTHOR CONTRIBUTION

Acquisition of data: Park YE, Kim JN, Lee NR, Cheon JH. Analysis and interpretation of data: Park YE. Drafting of the manuscript: Park YE. Study concept and design: Kim JN, Lee NR, Park Y, Park SJ, Kim TI, Kim WH, Cheon JH. Critical revision of the manuscript for important intellectual content: Park Y, Park SJ, Kim TI, Kim WH, Cheon JH. All authors approved the final version of the article, including the authorship list.

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SUPPLEMENTARY MATERIAL

Supplementary materials are available at the *Intestinal Research* website (https://www.irjournal.org).

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See "Is fasting beneficial for hospitalized patients with inflammatory bowel diseases?" on page 85-95.

Supplementary Table 1. Factors Involved in Reducing the CRP Levels (Cox Regression Analysis)

Variable	Univariate analysis		Multivariate analysis	
	P-value	HR (95% CI)	*P*-value	Adjusted HR (95% CI)
Male sex	0.856	0.972 (0.713–1.325)	0.656	1.091 (0.743–1.601)
Age at admission (yr)	0.558	1.003 (0.993–1.013)	0.018	0.982 (0.968–0.997)
Hospital stay (day)	0.007	1.013 (1.003–1.022)	0.520	1.004 (0.991–1.018)
Diet prescription				
Dietary group		1 (reference)		1 (reference)
Fasting group	0.469	0.893 (0.657–1.213)	0.213	0.793 (0.551–1.142)
Body weight (kg) at admission	0.363	0.992 (0.976–1.009)	0.503	1.007 (0.987–1.027)
BMI (kg/m^2)	0.830	0.995 (0.948–1.043)		
Process of admission				
Outpatient clinic		1 (reference)		1 (reference)
Emergency room	0.895	0.980 (0.722–1.329)	0.386	1.175 (0.816–1.691)
Type of IBD				
UC		1 (reference)		1 (reference)
CD	0.311	0.821 (0.560–1.202)	0.325	0.757 (0.434–1.318)
Intestinal Behçet's disease	0.289	1.231 (0.839–1.806)	0.726	1.091 (0.671–1.772)
Underlying disease				
Hypertension	0.140	1.495 (0.876–2.549)		
Diabetes	0.392	0.714 (0.330–1.545)		
Hematologic disorder	0.039	1.490 (1.020–2.176)	0.378	1.232 (0.775–1.959)
Laboratory findings				
Hemoglobin (g/dL)	0.005	0.917 (0.863–0.975)	0.971	1.002 (0.919–1.092)
Albumin (g/dL)	<0.001	0.639 (0.510–0.800)	0.017	0.686 (0.503–0.936)
ESR (mm/hr)	<0.001	1.009 (1.004–1.013)	0.004	1.009 (1.003–1.014)
Medications				
5-ASA	0.995	1.001 (0.642–1.562)	0.598	1.158 (0.671–1.998)
Corticosteroids	0.036	1.394 (1.021–1.902)	0.855	1.041 (0.675–1.606)
Immunomodulators	0.024	0.695 (0.507–0.954)	0.259	0.796 (0.536–1.183)
Anti-TNF agents	0.801	1.047 (0.731–1.501)	0.712	0.921 (0.594–1.428)
Others[a]	0.181	1.378 (0.861–2.204)	0.047	1.906 (1.010–3.598)
Nutritional support			-	-
TPN	0.057	1.578 (0.986–2.524)		
EN	0.737	1.086 (0.672–1.753)		

[a]Others: methotrexate, 6-mercaptopurine.
5-ASA, 5-aminosalicylic acid; TPN, total parenteral nutrition; EN, enteral nutrition.