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Original article

Isolated colonic Crohn's disease is associated with a reduced response to exclusive enteral nutrition compared to ileal or ileocolonic disease

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SUMMARY

Background & aims: Exclusive enteral nutrition (EEN) as a primary therapy is safe and effective for inducing the clinical remission of active luminal Crohn's disease (CD). Whether isolated colonic involvement affects the efficacy of EEN is controversial. We aimed to identify the influence of isolated colonic CD on the efficacy of EEN and to determine other potential predictors of the response to induction therapy with EEN in adult patients with CD.

Methods: Data for adult CD patients treated with EEN as an induction therapy at our centre from January 1, 2014, to May 31, 2017, were reviewed. Eligible patients were divided into an isolated colonic Crohn's disease (cCD) group and a non-isolated colonic Crohn's disease (non-cCD) group according to the disease location. The rates of clinical remission and inflammatory and nutritional serum markers were compared between the groups. Possible relationships between isolated colonic involvement or other potential factors and the efficacy of EEN were assessed by univariate and multivariate analyses. The propensity score matching method was used to confirm the results.

Results: Overall, 241 patients were included in the analysis: 52 patients in the cCD group and 189 patients in the non-cCD group. The rates of clinical remission differed between the two groups (cCD group: 51.9% versus non-cCD group: 68.3%, P = 0.029). Multivariate analyses indicated that isolated colonic involvement was associated with a reduced response to EEN (OR = 2.74; [CI] 95% = [1.2–6.23], P = 0.016). Additionally, the lean body mass index (LBMI) before treatment was associated with the efficacy of EEN (OR = 0.636; [CI] 95% = [0.444–0.912], P = 0.014). These associations were confirmed using the propensity score model. For patients with isolated colonic CD, multivariate analysis showed that pancolitis (OR = 16.7; [CI] 95% = [1.074–260.5], P = 0.044) was another independent factor for the efficacy of EEN. Further analysis showed that even in patients who achieved clinical remission after EEN, inflammatory serum markers declined more slowly in the cCD group than in the non-cCD group, and the time to remission was longer in the cCD group.

Conclusions: Isolated colonic CD showed a reduced response to induction therapy with EEN compared with ileal or ileocolonic disease in adult patients. Patients with isolated colonic CD required more time to benefit from EEN therapy compared with patients with non-colonic CD. Additionally, LBMI before treatment was associated with the efficacy of EEN.

1. Introduction

Exclusive enteral nutrition (EEN) as a primary therapy is safe and effective for inducing the remission of active luminal Crohn's disease (CD). Numerous studies have demonstrated that EEN can induce both clinical and endoscopic remission, benefit growth and nutritional status, and improve quality of life in children with CD [1–4]. Thus, EEN is recommended as the first-line therapy for

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paediatric patients with CD. Previous studies have also reported that EEN is effective in adult patients with CD. However, the use of EEN in adults is still debatable as the response rate to EEN in adults is extremely heterogeneous, ranging from 50 to 80% [1,5–7]. Therefore, the identification of factors associated with the response to EEN will help to optimize and personalize the use of EEN in clinical practice.

Given that isolated colonic Crohn's disease differs from other phenotypes of Crohn's disease in many aspects, such as genetics, intestinal microecology, and serological antibodies [8], the response of isolated colonic Crohn's disease to EEN is also believed to differ. There is a common belief among gastroenterologists that EEN is not as effective for isolated colonic Crohn's disease as it is for ileal or ileocolonic disease. However, evidence regarding the response of isolated colonic Crohn's disease to EEN treatment is limited and controversial. Moreover, most of the studies were conducted in children [6,9–12]. Two studies reported that children with isolated colonic disease had a worse response to EEN than those with small intestinal involvement, while the other studies showed no significant difference in remission rates between isolated colonic disease and disease at other sites. Data concerning the efficacy of EEN for isolated colonic Crohn's disease in adults are scarce [13].

The common consequences of CD are weight loss, exhaustion of energy reserves [14] and a significant decrease in lean body mass [15]. A strong association between lean body mass and prognosis has been reported for inflammatory bowel disease (IBD) [16–18], and it may be associated with patients' response to treatments [19]. Whether lean body mass is associated with the effectiveness of EEN remains unclear.

In the present study, we aimed to identify whether isolated colon involvement is an independent risk factor for failure to respond to induction therapy with EEN in adult patients with Crohn's disease. We also explored other clinical and serologic factors associated with the effects of induction therapy with EEN in adults with CD.

2. Methods

2.1. Patients and data collection

Approval was obtained from the institutional review board of Jinling Hospital. A retrospective analysis of a prospectively maintained database of all patients treated in the IBD centre at Jinling Hospital from January 1, 2014, to May 31, 2017, was performed. During this period, 613 patients with a diagnosis of CD were admitted to our centre. Among them, 241 who met the inclusion criteria and exclusion criteria were enrolled in this study. The inclusion criteria were as follows: 1. Age $\geq$18 years; 2. in the active disease phase (CRP $\geq$ 10 mg/L & Harvey–Bradshaw Index (HBI) > 4); 3. EEN as the primary induction therapy. The exclusion criteria were as follows: 1. presence of bowel stoma; 2. treatment with EEN as maintenance therapy. All the patients underwent colonoscopy and abdominal CT scan or small intestine imaging CT routinely during the first week of hospitalization, and gastroduodenoscopy was conducted if upper gastrointestinal disease was suspected. Blood tests and HBI scores were performed once a week to determine whether the patients achieved clinical remission. The following data were collected: age, sex, course of disease, family history of IBD in first-degree relatives, body mass index (BMI), Montreal classification, maintenance medication, history of surgery, serum inflammation biomarkers (C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR)), serum albumin (ALb) and haemoglobin (Hb).

2.2. EEN therapy

Patients were treated with EEN to induce clinical remission if they had no contraindications for EEN and met one of the following conditions: 1) patients with active luminal disease who agreed to receive EEN; 2) patients with active luminal disease and nutritional risk (Nutrition Risk Screen 2002 (NRS2002) score > 3). Any food and drink except water was forbidden. Daily caloric intake was 25–30 kcal/kg/d and gradually increased from half that amount to the full amount over 2 days. Patients received the EN via a nasogastric tube 24 h per day. All EN was prescribed by doctors, and the EN intake was recorded daily by professional nurses at our centre.

2.3. Body composition measurements

The body composition of the patients was estimated using a multifrequency bioelectrical impedance analyser (Biospace InBody Co., Korea) at admission. The patients were not allowed to eat or drink for 6 h before the test and were instructed to empty their bladder if possible. The patients stood barefoot on the detector with both the heel and forefoot on the foot electrodes and the hands holding the hand electrodes, with the upper limbs resting away from the torso. After the test, the fat and skeletal muscle mass, total lean mass, fat ratio, BMI and basal metabolic rate were accurately analysed. We then calculated the lean body mass index (LBMI) for every patient as the skeletal muscle mass (kg) divided by height squared (m^2).

2.4. Definitions

The diagnosis of CD was based on endoscopic, histological, and/or radiological findings according to the European evidence-based consensus on the diagnosis and management of Crohn's disease 2016 [20]. All patients were categorized into the isolated colonic Crohn's disease (cCD) group or the non-isolated colonic Crohn's disease (non-cCD) group according to their Montreal classification. The cCD group included patients with the involvement of any colonic location between the caecum and rectum but with no small bowel or upper gastrointestinal involvement. Clinical remission of CD was defined as a CRP level < 10 mg/L and HBI score $\leq$ 4. We considered EEN treatment to have failed to induce remission when one of the following conditions was met: 1. HBI >4 and/or CRP >10 mg/L after EEN treatment; 2. EEN treatment interference due to intolerance or non-compliance; 3. the patient required further treatment, such as surgery, corticosteroids or anti-TNFα or other medicine.

2.5. Statistical analysis

Statistical analysis was performed using SPSS version 23.0 (SPSS, Inc., an IBM Company, Chicago, IL). The quantitative and qualitative variables were expressed as the mean (SD), frequency and percentage. The *t* test was used to assess parametric data. The primary endpoint was clinical remission. To compare clinical remission rates, we used Pearson's chi-square analyses or Fisher's exact tests, as appropriate. To identify predictors of response to EEN treatment, we used univariate and multivariate analyses to examine the relationship between clinical remission and disease location and other variables. Because the response to EEN treatment was dependent on the patient and disease characteristics, a propensity score was calculated and introduced into the analyses of clinical remission using the nearest-neighbour matching method. $P < 0.05$ was considered significant.

3. Results

3.1. Patient characteristics

A total of 241 patients with active luminal CD were included in this study. The characteristics of the patients are summarized in Table 1. Among them, 158 (65.5%) were male, more than half (159/241, 65.9%) had a BMI <18.5 kg/m^2, and 151 (62%) were hospitalized due to abdominal pain and/or diarrhoea. The mean course of disease was 63.41 ± 52.11 months. In terms of disease location, 52 patients were in the cCD group, and the others were in the non-cCD group. Fifty-eight patients were treated with EEN at their initial diagnosis, and 22.4% (13/58) had isolated colonic involvement. The baseline characteristics were comparable between the two groups, excluding age (37.22 ± 11.98 vs 32.25 ± 13.69 years, P = 0.011) and disease behaviour (less B1 (non-stricturing & non-penetrating) in the non-cCD group, P = 0.002).

3.2. Clinical response to EEN

All patients received EEN treatment for more than 2 weeks. One hundred fifty-six patients (64.7%) achieved clinical remission after induction therapy with EEN. The clinical remission rate of the cCD group was much lower than that of the non-cCD group (51.9% vs 68.3%, P = 0.029) (Fig. 1). The mean HBI score and CRP level were 6.75 ± 1.67 and 46.8 ± 39.5 before treatment and 2.97 ± 0.9 and 6.09 ± 2.7 (P < 0.001) after treatment, respectively, among those who achieved clinical remission. Further details are presented in Table 2. Among those who did not respond well to EEN treatment, 10 patients in the cCD group underwent surgery, 8 patients switched to corticosteroids, 2 patients used anti-TNFα, and 5 patients in the cCD group did not seek further treatment for a specific reason. Thirty-six patients in the non-cCD group required surgery, 9 changed to corticosteroids, 8 used anti-TNFα therapy, and 9 discontinued treatment for other reasons, such as intolerance and poor compliance.

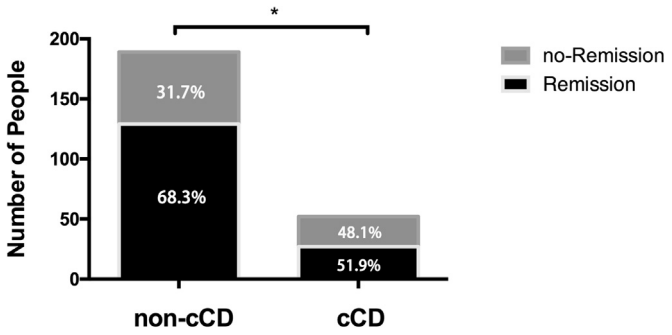

Fig. 1. Clinical remission with EEN therapy. The number of clinical remission patients in the cCD group was 27 (51.9%). The number of clinical remission patients in the non-cCD group was 129 (68.3%). cCD: isolated colonic Crohn's disease group; non-cCD: non-isolated colonic Crohn's disease group. *P < 0.05.

3.3. Univariate and multivariate analyses of factors influencing the clinical remission rate with EEN for all patients

The results of the univariate and multivariate analyses of the factors associated with the effects of EEN treatment in 241 patients are reported in Table 3. For all patients, isolated colonic disease was identified as an independent risk factor for failure to respond to EEN therapy (odds ratio [OR] = 2.74; confidence interval [CI] 95% = [1.2–6.23], P = 0.016). The CRP level before treatment (OR = 1.01; CI 95% = [1.003–1.017], P = 0.008) was also associated with the efficacy of EEN. Furthermore, the LBMI was a protective factor (odds ratio [OR] = 0.636; confidence interval [CI]

Table 1
Demographic data and disease characteristics of patients with Crohn's disease (CD) who received exclusive enteral nutrition (EEN) as primary therapy.

	All (n = 241)	cCD (n = 52)	non-cCD (n = 189)	P value
Age, years	36.15 ± 12.51	32.25 ± 13.69	37.22 ± 11.98	0.01
Sex, male, n (%)	158 (65.50)	31 (59.60)	127 (67.20)	0.30
BMI	18.02 ± 10.74	17.9 ± 3.3	18.05 ± 12.02	0.30
Course of disease (months)	63.41 ± 52.11	58.86 ± 43.4	64.66 ± 54.3	0.47
Montreal classification, n (%)				
Behaviour				
B1	30 (12.4)	13 (25)	17 (9)	0.01
B2	92 (38.2)	19 (36.5)	73 (38.6)	0.75
B3	119 (49.3)	20 (38.5)	99 (52.4)	0.08
P	70 (29)	15 (28.8)	55 (29.1)	0.97
Smoking, n (%)	19 (7.89)	4 (7.7)	15 (7.9)	0.94
Duration of EEN (days)	26.5 ± 13.2	29.52 ± 14.2	25.76 ± 12.89	0.08
Maintenance medication, n (%)				
Sulfasalazine	9 (3.73)	3 (5.77)	6 (3.17)	0.38
Mesalazine	68 (28.2)	8 (15.4)	60 (31.7)	0.02
Azathioprine	72 (29.87)	10 (19.2)	62 (32.8)	0.06
Thalidomide	18 (7.5)	6 (11.5)	12 (6.3)	0.21
Tripterygium	15 (6.22)	3 (5.77)	12 (6.3)	0.88
None	59 (24.5)	22 (42.3)	37 (19.6)	<0.001
Corticosteroid history, n (%)	79 (32.78)	16 (30.77)	63 (33.33)	0.73
Surgery history, n (%)	101 (41.9)	23 (44.23)	78 (41.27)	0.70
Before-HBI	7.24 ± 2.08	7.23 ± 2.41	7.24 ± 1.99	0.96
Before-CRP (mg/L)	51.15 ± 43.19	48.7 ± 53.81	52.8 ± 42	0.56
Before-Alb (g/L)	36.5 ± 6.17	36.5 ± 5.8	36.4 ± 6.2	0.97
Before-LBMI	7.80 ± 1.5	8.05 ± 1.73	7.74 ± 1.42	0.20

Skeletal muscle/height^2, kg/m^2.
cCD: isolated colonic Crohn's disease group; non-cCD: non-isolated colonic Crohn's disease group; L1: isolated terminal ileal disease; L2: isolated colonic disease; L3: ileocolonic disease. L4; oesophagogastroduodenal disease & jejunal/proximal ileal disease; B1: non-stricturing non-penetrating; B2: stricturing; B3: penetrating; P: perianal lesions; HBI: Harvey–Bradshaw index; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; Hb: haemoglobin; ALb: albumin; LBMI: lean body mass index. Data are shown as the mean (SD).

Table 2
Changes in HBI and CRP levels before and after EEN treatment in the two groups.

			Before	After	P
cCD	Remission	HBI	6.2 ± 1.3	3.04 ± 0.64	<0.001
		CRP (mg/L)	36.15 ± 7.1	6.86 ± 1.32	0.001
	No remission	HBI	8.4 ± 2.8	6.0 ± 1.48	<0.001
		CRP (mg/L)	54.28 ± 52.46	30.4 ± 34.5	0.062
non-cCD	Remission	HBI	6.8 ± 1.72	2.87 ± 0.92	<0.001
		CRP (mg/L)	49.05 ± 39.83	5.9 ± 0.46	<0.001
	No remission	HBI	8.05 ± 2.31	5.43 ± 1.23	<0.001
		CRP (mg/L)	61.08 ± 47.45	27.07 ± 30.6	<0.001

cCD: isolated colonic Crohn's disease group; non-cCD: non-isolated colonic Crohn's disease group; HBI: Harvey–Bradshaw index; CRP: C-reactive protein. Data are shown as the mean (SD).

95% = [0.444–0.912], P = 0.014) for the efficacy of EEN. We then calculated the ROC curve for the CRP level and the LBMI for the cut-off value. The results showed that the cut-off value for the CRP level was 33.5 mg/L (sensitivity = 65%, specificity = 50%, positive predictive value = 72%, negative predictive value = 41%, AUC = 0.57), and the cut-off value for the LBMI was 7.47 kg/m^2 (sensitivity = 70%, specificity = 60%, positive predictive value = 76%, negative predictive value = 52%, AUC = 0.67).

To better assess the role of isolated colonic disease in the response to EEN therapy, a propensity score was calculated using the nearest-neighbour matching method. The adjustment for isolated colonic disease remained associated with an increased risk of failure of induction therapy with EEN (OR = 4.51; CI 95% = [1.41–14.42], P = 0.011). The LBMI was also associated with the response to EEN (OR = 0.669; CI 95% = [0.462–0.969], P = 0.033).

3.4. cCD responds slowly to EEN

We also compared the time required for the patients to achieve clinical remission (Fig. 2). The mean remission time was 31.5 ± 8.9 days in the cCD group and 25.6 ± 8.6 days in the non-cCD group (P = 0.001). These results indicated that patients with isolated colon involvement required a longer duration of EEN induction therapy to achieve clinical remission. We then evaluated the levels of HBI, CRP, ESR, Alb & Hb in patients with clinical remission (Fig. 3). We found that although the CRP levels in both groups declined over

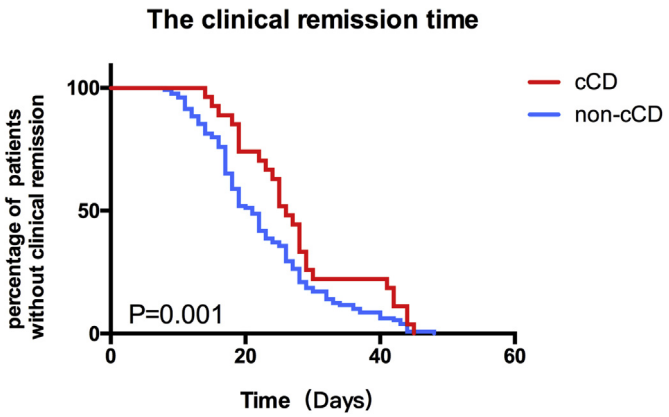

Fig. 2. Kaplan–Meier analysis of the time until clinical remission in the cCD group and the non-cCD group.

time, the △CRP in the remission patients in the non-cCD group showed a significant decrease (23.4 ± 33.8 mg/L, P < 0.001) in the first week, while there was no significant difference in the cCD group (11.1 ± 3.4 mg/L, P = 0.102). The nutrition data revealed a tendency to decline and then improve, and all the patients reverted to the original level or better after 3 weeks.

3.5. Univariate and multivariate analyses of factors influencing the clinical remission rate with EEN in the cCD group

Although the cCD group showed a reduced response to EEN compared with the non-cCD group, the rate of remission was greater than 50%. We also conducted univariate and multivariate analyses of factors associated with the efficacy of EEN treatment in the cCD group (Table 4.). The LBMI (odds ratio [OR] = 0.21; confidence interval [CI] 95% = [0.06–0.81], P = 0.022) and CRP level before treatment (odds ratio [OR] = 1.03; confidence interval [CI] 95% = [1.001–1.05], P = 0.049) were identified as independent factors related to the response to EEN. Additionally, we observed a poor response to EEN in cases of pancolitis (from caecum to rectum) compared with segmental colitis (odds ratio [OR] = 16.7; confidence interval [CI] 95% = [1.074–260.5], P = 0.044).

Table 3
Univariate and multivariate analysis of risk factors for the clinical remission rate with EEN.

	Univariate analysis			Multivariate analysis	
	Remission (n = 156)	No remission (n = 85)	P	Odds ratio (95% CI)	P
cCD	27 (17.3)	25 (29.4)	0.031	2.74 (1.2–6.23)	0.016
Male	108 (69.2)	50 (58.8)	0.105	–	
Age	36.97 ± 12.47	34.64 ± 12.51	0.166	–	
BMI	18.74 ± 13.18	16.70 ± 2.65	0.009	0.98 (0.827–0.155)	0.786
Course of disease	67.6 ± 55.22	55.72 ± 45.16	0.094	0.994 (0.987–1.002)	0.126
New diagnosis	37 (23.7)	21 (24.7)	0.937	–	
Behaviour					
B1	19 (12.2)	11 (12.9)	1	–	
B2	62 (39.7)	30 (35.3)	0.975	–	
B3	75 (48.1)	44 (51.8)	0.510	–	
P	53 (34.0)	17 (20)	0.024	0.611 (0.284–1.315)	0.208
Smoking	15 (9.6)	4 (4.7)	0.178	–	
Corticosteroid history	49 (31.4)	30 (35.3)	0.54	–	
Before-CRP (mg/L)	46.82 ± 39.53	59.08 ± 48.46	0.038	1.01 (1.003–1.017)	0.008
Before-Alb (g/L)	36.6 ± 6.22	36.33 ± 6.13	0.748	–	
Before-ESR (mm/h)	40.61 ± 26.67	46.41 ± 31.95	0.135	–	
Before-LBMI	8.07 ± 1.37	7.27 ± 1.60	0.001	0.636 (0.444–0.912)	0.014

EEN: exclusive enteral nutrition; cCD: isolated colonic Crohn's disease group; B1: non-stricturing non-penetrating; B2: stricturing; B3: penetrating; P: perianal lesions; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; Hb: haemoglobin; ALb: albumin; LBMI: lean body mass index. Data are shown as the mean (SD) & n (%).

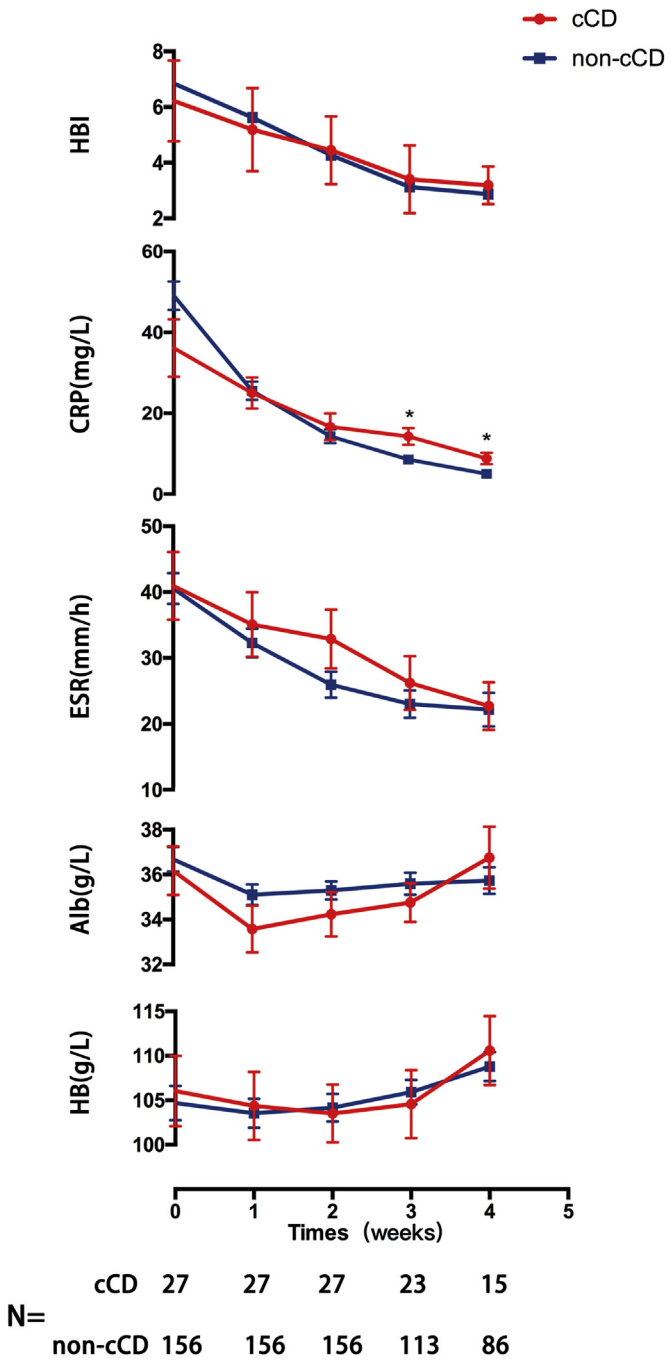

Fig. 3. HBI, CRP, ESR, Hb, and Alb levels in patients with clinical remission after EEN treatment. HBI: Harvey–Bradshaw index; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; Hb: haemoglobin; ALb: albumin. N is the number of patients who were treated with EEN at each time point. *P < 0.05.

4. Discussion

The effectiveness of EEN therapy for inducing clinical remission in adult patients with CD is controversial, especially for those with isolated colonic involvement. This study provided evidence that in adults, isolated colonic CD does not respond as well as other phenotypes of CD to EEN therapy. In the present study, the clinical remission rate in the cCD group was 51.9% compared with 68.3% in the non-cCD group, which is similar to the reports of Afzal et al. [10] and De Bie et al. [6] but much lower than the findings reported by Buchanan et al. [11], who used the Vienna classification and genotype-phenotype analysis to classify paediatric CD, which might have influenced the final statistics.

In this study, although the cCD group responded less well to EEN, the response rates were greater than 50%, which is similar to (or better than) the response rates observed with various drug therapies. We obtained several meaningful results. First, the patients in the cCD group required more time to achieve clinical remission: It took approximately one week to decrease the inflammatory serum markers (e.g., CRP) and HBI to the normal level in the cCD group compared with the non-cCD group. Additionally, we observed that the patients in the non-cCD group who achieved clinical remission had a much greater decrease in CRP concentration than those in the cCD group, indicating that EEN had a reduced anti-inflammatory effect in adults with isolated colonic involvement. These results indicate that cCD patients required more time to benefit from EEN. Second, we found that pancolitis may influence the efficacy of EEN therapy in adult patients with isolated CD. A probable explanation is that pancolitis is often associated with more severe disease and a higher inflammatory state. The effect of immunonutrition and anti-inflammation may be restricted by the massive presence of inflammatory cytokines in the bodies of the patients with isolated colon CD, an explanation that compares favourably with the findings of Souza HS et al. [21] of a poor response of colon cobblestoning in adults to treatment with enteral nutrition. Third, the LBMI before treatment was a favourable predictor of the efficacy of EEN therapy. Some research has shown a significantly lower lean body mass in patients with high disease activity than in those with mild to moderate disease activity [22]. Moreover, a strong association between sarcopenia and prognosis has been reported in the field of IBD [16–18]. Thus, it is conceivable that LBMI could be predictive of the response to EEN. On the one hand, the formula for LBMI is similar to that for BMI, which can preclude individual differences. On the other hand, LBMI can precisely reflect the severity of CD. We believe that LBMI, as a reflection of both nutritional status and the inflammatory condition, plays an important role in predicting the response to EEN treatment.

Although the positive effects of EEN in adult CD patients have been accepted, there are still some unclear explanations for how EEN reduces bowel inflammation. The absence of alloantigens, such as titanium dioxide, which is widely used in food as a whitener, may reduce the antigenic pressure on the intestine (a phenomenon called 'bowel rest'); [23] however, this cannot explain the different clinical remission rates between the cCD group and non-cCD groups. A second explanation may be that EEN modulates the bacterial flora within the gut lumen. Recent data indicate that the dysbiotic microbiota in isolated colonic CD has distinct characteristics and that the interaction of bacteria influences the catabolism and absorption of EEN and leads to reduced intestinal inflammation [24–26]. A third possible explanation is that EEN has direct anti-inflammatory effects on intestinal epithelial cells by down-regulating mucosal pro-inflammatory cytokines [27,28]. Finally, as we mentioned previously, LBMI can predict the response of EEN, the improvement of nutritional status by remediating nutritional deficiencies is likely to contribute to the benefits seen with EEN [29].

Our study had several limitations, including its retrospective design, which might have affected the outcomes. Additionally, the recording of blood data was limited to 4 weeks and thus might not clearly reflect the tendency to change. Third, we did not record BMI data for each week, which might have led to an incomplete assessment of nutrition status. Finally, all patients were from the same nation, and most were of Han Chinese descent.

In conclusion, isolated colonic involvement was an independent risk factor for a poor response to EEN induction therapy in

Table 4
Univariate and multivariate analysis of risk factors for clinical remission with EEN in the cCD group.

	Univariate analysis			Multivariate analysis	
	Remission (n = 27)	No remission (n = 25)	P	Odds ratio (95% CI)	P
Male	19 (70.3)	12 (48)	0.104	–	
Age	31.4 ± 12.8	33 ± 14.8	0.681	–	
BMI	19.6 ± 3.1	15.9 ± 2.3	0.001	0.87 (0.58–1.30)	0.500
Course of disease (mon)	46.6 ± 28.3	67.7 ± 51	0.084	1.01 (0.99–1.03)	0.460
New diagnosis	7 (25.9)	6 (24)	0.873	–	
Behaviour					
B1	7 (25.9)	6 (24)	1	–	
B2	11 (40.7)	8 (32)	0.877	–	
B3	9 (33.4)	11 (44)	0.589	–	
P	10 (37)	5 (20)	0.181	–	
Smoking	2 (7.4)	2 (4)	0.936	–	
Corticosteroid history	8 (29.6)	8 (32)	0.853	–	
Before-CRP (mg/L)	36.15 ± 36.8	62.8 ± 35	0.097	1.03 (1.001–1.05)	0.049
Before-Alb (g/L)	36.6 ± 6.22	36.33 ± 6.13	0.637	–	
Before-ESR (mm/h)	40.9 ± 26.8	40.7 ± 29	0.979	–	
Before-LBMI	8.9 ± 1.22	6.98 ± 1.48	0.007	0.21 (0.06–0.81)	0.022
Pancolitis	2 (7.5)	12 (48)	0.003	16.7 (1.07–260.5)	0.044
Antibiotics	5 (18.5)	7 (28)	0.420	–	

cCD: isolated colonic Crohn's disease group; B1: non-stricturing non-penetrating; B2: stricturing; B3: penetrating; P: perianal lesions; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; Hb: haemoglobin; ALb: albumin; LBMI: lean body mass index. Data are shown as the mean (SD) & n (%).

adults with CD. The remission rate was lower in the cCD group than in the non-cCD group. Patients with isolated colonic disease responded slowly to EEN and required a longer time to achieve remission. In addition, a high LBMI had a strong association with an effective response to EEN treatment for all phenotypes of CD, indicating that body composition, especially lean body mass, might be a predictive factor for clinical remission with EEN therapy. For adult patients with isolated colonic CD, pancolitis was an independent predictor of a reduced response to EEN. However, further prospective research with a larger number of patients is needed to confirm our results.

Statement of authorship

This study was conducted at the IBD Centre, Jinling Hospital, and approval from the institutional review board of Jinling Hospital was obtained.

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Conflict of interest

The authors confirm that there are no conflicts of interest to declare.

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Yihan Xu, Zhen Guo and Lei Cao contributed equally to this work. Weiming Zhu supervised the entire project. Lei Cao collected the data, and Jianfeng Gong analysed the dataset. Yihan Xu and Zhen Guo conducted the data analyses and drafted the manuscript. All the authors critically reviewed the article and approved the final manuscript.

References

[1] Grover Z, Muir R, Lewindon P. Exclusive enteral nutrition induces early clinical, mucosal and transmural remission in paediatric Crohn's disease. J Gastroenterol 2014;49:638–45.
[2] Hill RJ. Update on nutritional status, body composition and growth in paediatric inflammatory bowel disease. World J Gastroenterol 2014;20:3191–7.
[3] Forbes A, Escher J, Hébuterne X, Kłęk S, Krznaric Z, Schneider S, et al. ESPEN guideline: clinical nutrition in inflammatory bowel disease. Clin Nutr 2017;36:321–47.
[4] Yamamoto T, Nakahigashi M, Umegae S, Kitagawa T, Matsumoto K. Impact of long-term enteral nutrition on clinical and endoscopic recurrence after resection for Crohn's disease: a prospective, non-randomized, parallel, controlled study. Aliment Pharmacol Ther 2006;25:67–72.
[5] Levine A, Wine E. Effects of enteral nutrition on Crohn's disease: clues to the impact of diet on disease pathogenesis. Inflamm Bowel Dis 2013;19:1322–9.
[6] De Bie C, Kinderman A, Escher J. Use of exclusive enteral nutrition in paediatric Crohn's disease in The Netherlands. J Crohn's Colitis 2013;7:263–70.
[7] Johnson T, Macdonald S, Hill SM, Thomas A, Murphy MS. Treatment of active Crohn's disease in children using partial enteral nutrition with liquid formula a randomized controlled trial. Gut 2006;55:356–61.
[8] Subramanian S, Ekbom A. Recent advances in clinical practice: a systematic review of isolated colonic Crohn's disease: the third IBD? Gut 2017;66:362–81.
[9] Wilschanski M, Sherman P, Pencharz P, Davis L, Corey M, Griffiths A. Supplementary enteral nutrition maintains remission in paediatric Crohn's disease. Gut 1996;38:543–8.
[10] Afzal Nadeem A, Davies Sue, Paintin Morine, Arnaud-Battandier Franck, Walker-Smith John A, Murch Simon, et al. Colonic Crohn's disease in children does not respond well to treatment with enteral nutrition if the ileum is not involved. Dig Dis Sci 2005;50:1471–5.
[11] Buchanan E, Gaunt WW, Cardigan T, Garrick V, McGrogan P, Russell RK, et al. The use of exclusive enteral nutrition for induction of remission in children with Crohn's disease demonstrates that disease phenotype does not influence clinical remission. Aliment Pharmacol Ther 2009;30:501–7.
[12] Rubio A, Pigneur B, Garnier-Lengliné H, Talbotec C, Schmitz J, Canioni D, et al. The efficacy of exclusive nutritional therapy in paediatric Crohn's disease, comparing fractionated oral vs. continuous enteral feeding. Aliment Pharmacol Ther 2011;33:1332–9.
[13] Lochs H, Steinhardt HJ, Klaus-Wentz B, Zeitz M, Vogelsang H, Sommer H, et al. Comparison of enteral nutrition and drug treatment in active Crohn's disease. Results of the European Cooperative Crohn's Disease Study. IV. Gastroenterology 1991;101:881–8.
[14] Jahnsen J, Falch JA, Mowinckel P, Aadland E. Body composition in patients with inflammatory bowel disease: a population-based study. Am J Gastroenterol 2003;98:1556–62.
[15] Azcue M, Rashid M, Griffiths A, Pencharz PB. Energy expenditure and body composition in children with Crohn's disease: effect of enteral nutrition and treatment with prednisolone. Gut 1997;41:203–8.
[16] Schneider SM, Al-Jaouni R, Filippi J, Wiroth JB, Zeanandin G, Arab K, et al. Sarcopenia is prevalent in patients with Crohn's disease in clinical remission. Inflamm Bowel Dis 2008;14:1562–8.
[17] Zhang T, Cao L, Cao T, Yang J, Gong J, Zhu W, et al. Prevalence of sarcopenia and its impact on postoperative outcome in patients with Crohn's disease undergoing bowel resection. J Parenter Enteral Nutr 2017;41:592–600.
[18] Bamba S, Sasaki M, Takaoka A, Takahashi K, Imaeda H, Nishida A, et al. Sarcopenia is a predictive factor for intestinal resection in admitted patients with Crohn's disease. PLoS One 2017;12:e0180036.

[19] Shen W, Cao L, Li Y, Cai X, Ge Y, Zhu W. Visceral fat is associated with mucosal healing of infliximab treatment in Crohn's disease. Dis Colon Rectum 2018;61:706–12.
[20] Gomollón F, Dignass A, Annese V, Tilg H, Van Assche G, Lindsay JO, et al. 3rd European evidence-based consensus on the diagnosis and management of Crohn's disease 2016: part 1: diagnosis and medical management. J Crohn's Colitis 2017;11:3–25.
[21] Souza HS, Carvalho AT, Madi K, Silva JR, Elia CS. Phenotypic analysis of intestinal non–inflamed mucosa in Crohn's disease: evidence of mononuclear cell depletion in lamina propria. Eur J Gastroenterol Hepatol 1996;8(6):563–8.
[22] Yan T, Li L, Wu Q, Gao X, Hu P, He Q. Analysis of body composition in patients with Crohn's disease. Zhonghua Wei Chang Wai Ke Za Zhi 2014;17:981–4.
[23] Lomer MC, Hutchinson C, Volkert S, Greenfield SM, Catterall A, Thompson RP, et al. Dietary sources of inorganic microparticles and their intake in healthy subjects and patients with Crohn's disease. Br J Nutr 2004;92:947–55.
[24] Lopez-Siles M, Martinez-Medina M, Busquets D, Sabat-Mir M, Duncan SH, Flint HJ, et al. Mucosa-associated *Faecalibacterium prausnitzii* and Escherichia coli co-abundance can distinguish irritable bowel syndrome and inflammatory bowel disease phenotypes. Int J Med Microbiol 2014;304:464–75.
[25] Naftali T, Reshef L, Kovacs A, Porat R, Amir I, Konikoff FM, et al. Distinct microbiotas are associated with ileum-restricted and colon-involving Crohn's disease. Inflamm Bowel Dis 2016;22:293–302.
[26] Haberman Y, Tickle TL, Dexheimer PJ, Kim MO, Tang D, Karns R, et al. Pediatric Crohn's disease patients exhibit specific ileal transcriptome and microbiome signature. J Clin Investig 2014;124:3617–33.
[27] Fell JM, Paintin M, Arnaud-Battandier F, Beattie RM, Hollis A, Kitching P, et al. Mucosal healing and a fall in mucosal pro-inflammatory cytokine mRNA induced by a specific oral polymeric diet in paediatric Crohn's disease. Aliment Pharmacol Ther 2000;14:281–9.
[28] Yamamoto T, Nakahigashi M, Umegae S, Kitagawa T, Matsumoto K. Impact of elemental diet on mucosal inflammation in patients with active Crohn's disease: cytokine production and endoscopic and histological findings. Inflamm Bowel Dis 2005;11:580–8.
[29] Heuschkel R. Enteral nutrition should be used to induce remission in childhood Crohn's disease. Dig Dis 2009;27:297–305.