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Original Article

Factors Associated with Reaching Mid-Parental Height in Patients Diagnosed with Inflammatory Bowel Disease in Childhood and Adolescent Period

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Background/Aims: The recent update on the Selecting Therapeutic Targets in Inflammatory Bowel Disease initiative has added normal growth in children as an intermediate target in Crohn's disease and ulcerative colitis. We aimed to investigate factors associated with reaching mid-parental height (MPH) in patients diagnosed with inflammatory bowel disease in childhood and the adolescent period.

Methods: This multicenter retrospective observational study included pediatric patients with inflammatory bowel disease that had reached adult height. Factors associated with reaching MPH were investigated by logistic regression analyses.

Results: A total of 166 patients were included in this study (128 Crohn's disease and 38 ulcerative colitis). Among them, 54.2% (90/166) had reached their MPH. Multivariable logistic regression analysis revealed that height Z-score at diagnosis and MPH Z-score were independently associated with reaching MPH (odds ratio [OR], 8.45; 95% confidence interval [CI], 4.44 to 17.90; p<0.001 and OR, 0.11; 95% CI, 0.04 to 0.24; p<0.001, respectively). According to the receiver operating characteristic curve analysis, the optimal cutoff level of "height Z-score at diagnosis minus MPH Z-score" that was associated with reaching MPH was –0.01 with an area under the curve of 0.889 (95% CI [0.835 to 0.944], sensitivity 88.9%, specificity 84.2%, positive predictive value 87.0%, negative predictive value 86.5%, p<0.001).

Conclusions: Height Z-score at diagnosis and MPH Z-score were the only factors associated with reaching MPH. Efforts should be made to restore growth in pediatric patients who present with a negative "height Z-score at diagnosis minus MPH Z-score." **(Gut Liver 2024;18:106-115)**

Key Words: Inflammatory bowel disease; Crohn disease; Ulcerative colitis; Height; Child

INTRODUCTION

Impairment of growth is one of the major complications occurring in 15% to 40% of patients with pediatric inflammatory bowel disease (IBD), and it is a factor that greatly affects the quality of life of patients.[1,2] The recent update on the Selecting Therapeutic Targets in Inflammatory Bowel Disease initiative has added normal growth in children as an intermediate target in Crohn's disease (CD) and ulcerative colitis (UC).[3] Efforts to achieve normal growth are

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important in pediatric IBD patients diagnosed at a time of growth and development.

Several factors contribute to the pathogenesis of growth impairment in children with IBD, including nutritional deficiencies due to insufficient intake and malabsorption, increased nutrient requirements and losses due to relative catabolism, genetic factors, corticosteroid uses and disease-related factors. Successful treatment of active disease can lead to normalization of height growth. Therefore, uncontrolled inflammation is a major cause of growth impairment in children with IBD, and in fact pro-inflammatory cytokines are also implicated in growth inhibition mechanisms.[4,5] However, there are some patients who do not grow well even after treatment for IBD, which shows that inflammation control alone cannot explain the persistent growth failure.

Although there have been many studies on growth impairment at the time of diagnosis or growth rate retardation in the first few years after diagnosis in children with IBD, studies on final adult height are still lacking. Few studies have looked at factors that potentially affect final adult height. Although there have been prior studies of adult and target heights, most height data were not as accurate as those measured by appropriately trained personnel.[6,7]

The purpose of this study was to compare the observed final adult height and the target height based on parental height, and to investigate factors associated with reaching mid-parental height (MPH) in patients diagnosed with IBD in childhood and adolescent period.

MATERIALS AND METHODS

1. Patients and data collection

This retrospective observational study was conducted between December 2021 and August 2022 at the department of pediatrics of eight centers in the Republic of Korea; Kyungpook National University Children's Hospital affiliated to Kyungpook National University Chilgok Hospital, Pusan National University Children's Hospital affiliated to Pusan National University Yangsan Hospital, Kosin University Gospel Hospital, Yeungnam University Medical Center, Samsung Changwon Hospital, Gyeongsang National University Hospital, Gyeongsang National University Changwon Hospital, and Keimyung University Dongsan Hospital.

Pediatric-onset IBD patients who had been diagnosed under 18 years of age and had reached their final adult height were included in this study. Final adult height was defined as a stable height for more than 6 months in those over 18 years of age. Those without documented paternal and maternal height were excluded. CD and UC were diagnosed in accordance with the revised Porto criteria of the European Society for Paediatric Gastroenterology, Hepatology, and Nutrition.[8] Disease phenotype was classified according to the Paris classification.[9]

Baseline demographic and clinical data, including sex, diagnosis age, disease type, growth indicators, paternal and maternal height, Tanner stage, family history of IBD, laboratory results at diagnosis including white blood cell count, hematocrit, platelet count, serum albumin level, erythrocyte sedimentation rate, C-reactive protein, fecal calprotectin levels, disease phenotype according to the Paris classification, disease activity scores including Pediatric Crohn's Disease Activity Index and Pediatric Ulcerative Colitis Activity Index were obtained from electronic medical records.[10,11] At follow-up, final adult height, use of medications including corticosteroids, exclusive enteral nutrition, immunomodulators, anti-tumor necrosis factor agents, relapse during treatment were investigated.

2. Study design and definition

Comparative analysis was conducted between groups divided according to whether the patient had reached his or her MPH, which was calculated according to the following formula[12] which is as follows:

$$\text{MPH for boys (cm)} = \frac{(\text{Paternal height} + \text{Maternal height} + 13)}{2}$$

$$\text{MPH for girls (cm)} = \frac{(\text{Paternal height} + \text{Maternal height} + 13)}{2}$$

All growth indices, including z-scores for weight-for-age, height-for-age, and body mass index-for-age, and final expected were values derived using the 2017 Korean National Growth Charts for children and adolescents of the Korean Centers for Disease Control and Prevention.[13] Additional comparative analysis was performed by dividing the CD patients into groups according to whether the patient had reached his or her MPH or not.

3. Statistical analysis

For comparative analysis between groups, the chi-square test or Fisher exact test were used for categorical variables, and the Student t-test or Wilcoxon rank-sum test were used for continuous variables. Continuous variables were reported as median of the interquartile range or the mean of the standard deviation. Univariate and multivariate logistic regression analyses were used to identify factors associated with reaching MPH. Univariate logistic regres-

sion analysis was performed to determine the crude odds ratio (OR) for each factor, and factors with a p-value <0.1 in the univariate analysis were included in the multivariate analysis. Results were expressed as adjusted ORs with 95% confidence intervals (CIs). In addition, receiver operating characteristic curve analysis was performed to derive the most accurate cutoff points for continuous variables associated with reaching MPH. The results were expressed as the area under the curve with 95% CIs, and sensitivity, specificity, positive predictive value, and negative predictive value were calculated. Statistical significance was defined as p<0.05. All analyses were performed with SAS software version 9.4 (SAS Institute, Cary, NC, USA).

Table 1. Baseline Characteristics

Characteristic	Type	Value (n=166)
Male sex, No. (%)		111 (66.9)
Age at diagnosis, median (IQR), yr		14.9 (13.2 to 16.5)
IBD disease type, No. (%)	Crohn's disease	128 (77.1)
	Ulcerative colitis	38 (22.9)
Height Z-score at diagnosis, mean±SD		–0.18±1.03
Weight Z-score at diagnosis, mean±SD		–0.74±1.22
BMI Z-score at diagnosis, median (IQR)		–0.87 (–1.65 to –0.02)
MPH Z-score, mean±SD		–0.27±0.68
Height Z-score at diagnosis minus MPH Z-score, mean±SD		0.09±1.00
Tanner stage, No. (%)	1	19 (11.4)
	2	23 (13.9)
	3	27 (16.3)
	4	33 (19.9)
	5	64 (38.6)
1st degree family history of IBD, No. (%)		7 (4.2)
White blood cell count, median (IQR), /μL		9,380 (6,810 to 11,400)
Hematocrit, mean±SD, %		36.3±5.4
Platelet count, median (IQR), $\times 10^3/\mu L$		421 (336 to 528)
Albumin, median (IQR), g/dL		3.8 (3.3 to 4.3)
Erythrocyte sedimentation rate, median (IQR), mm/hr		40 (20 to 66)
C-reactive protein, median (IQR), mg/dL		2.77 (0.60 to 5.94)
Fecal calprotectin, median (IQR), mg/dL		1,148 (457 to 2,000)
Crohn's disease (n=128)		
PCDAI, median (IQR)		40 (30 to 47.5)
Paris–lower GI tract involvement, No. (%)	L1	12 (9.4)
	L2	14 (10.9)
	L3	102 (79.7)
Paris–upper GI tract involvement, No. (%)	None	48 (37.5)
	L4a	41 (32.0)
	L4b	20 (15.6)
	L4a+b	19 (14.9)
Paris–luminal disease behavior, No. (%)	B1	85 (66.4)
	B2	28 (21.9)
	B3/B2B3	15 (11.7)
Paris–perianal disease modifier, No. (%)	No	57 (44.5)
	Yes	71 (55.5)
Ulcerative colitis (n=38)		
PUCAI, median (IQR)		45 (30 to 55)
Paris–disease extent, No. (%)	E1	8 (21.0)
	E2	6 (15.8)
	E3	2 (5.3)
	E4	22 (57.9)

IQR, interquartile range; IBD, inflammatory bowel disease; BMI, body mass index; MPH, mid-parental height; PCDAI, Pediatric Crohn's Disease Activity Index; GI, gastrointestinal; L1, distal 1/3 ileum±limited cecal disease; L2, colonic disease; L3,ileocolonic disease; L4a, upper disease proximal to ligament of Treitz; L4b, upper disease distal to the ligament of Treitz and proximal to the distal 1/3 ileum; L4a+b, upper disease involvement in both L4a and L4b; B1, nonstricturing nonpenetrating behavior; B2, stricturing behavior; B3, penetrating behavior; B2B3, both stricturing and penetrating behavior; PUCAI, Pediatric Ulcerative Colitis Activity Index; E1, ulcerative proctitis; E2, left-sided UC (distal to splenic flexure); E3, extensive (hepatic flexure distally); E4, pancolitis (proximal to hepatic flexure).

4. Ethics statement

This study was approved by the Institutional Review Board of Kyungpook National University Chilgok Hospital and informed consent was waived due to the retrospective nature of this study (IRB number: 2021-11-026).

RESULTS

1. Baseline characteristics

Overall, 166 patients were included in this study. Among them, 128 patients (77.1%) had been diagnosed with CD, and 38 patients (22.9%) with UC. Males comprised 66.9% (111/138) of the patients and the median age at diagnosis was 14.9 years (interquartile range, 13.2 to 16.5 years). Height Z-score at diagnosis was −0.18±1.03, and the MPH Z-score was −0.27±0.68. Other baseline demographics and clinical characteristics are summarized in Table 1.

2. At follow-up

The median age at follow-up was 19.9 years (interquar tile range, 18.8 to 21.7 years). Final adult height Z-score was –0.17±0.96, and 54.2% of the patients (90/166) had achieved MPH. Use of medications during treatment and relapse are summarized in Table 2.

3. Factors associated with reaching MPH

Comparative analysis between patients who had and had not reached MPH revealed that height Z-score at diagnosis, and MPH Z-score were the only factors that were significantly different between the two groups (Table 3).

According to logistic regression analyses, height Z-score at diagnosis and MPH Z-score were independently associated with reaching MPH (OR, 8.45; 95% CI, 4.44 to 17.90; p<0.001 and OR, 0.11; 95% CI, 0.04 to 0.24; p<0.001, respectively) (Table 4). According to the receiver operating characteristic curve analysis, the optimal cutoff level of "height Z-score at diagnosis minus MPH Z-score" that was associated with reaching MPH was –0.01 with an area under the curve of 0.889 (95% CI [0.835 to 0.944], sensitivity 88.9%, specificity 84.2%, positive predictive value 87.0%, negative predictive value 86.5%, p<0.001) (Fig. 1A).

4. Factors associated with reaching MPH among patients with CD

Further analyses were conducted among patients with CD. Comparative analysis between patients who had and had not reached MPH revealed that height Z-score at diagnosis, and MPH Z-score were the only factors that were significantly different between the two groups (Table 5).

According to logistic regression analyses, height Z-score at diagnosis and MPH Z-score were independently associated with reaching MPH (OR, 6.94; 95% CI, 3.49 to 15.66; p<0.001 and OR, 0.14; 95% CI, 0.05 to 0.34; p<0.001, respectively) (Table 6). According to the receiver operating characteristic curve analysis, the optimal cutoff level of "height Z-score at diagnosis minus MPH Z-score" that was associated with reaching MPH was –0.22 with an area under the curve of 0.874 (95% CI [0.808 to 0.941], sensitivity

Table 2. Clinical Data at Follow-up

Variable	Value (n=166)
Age at follow-up, yr	19.9 (18.8–21.7)
Use of corticosteroids during treatment	65 (39.2)
Use of EEN during treatment	63 (59.9)
Use of immunomodulator during treatment	159 (95.8)
Use of anti-TNF agents during treatment	127 (76.5)
Duration from diagnosis to initiation of anti-TNF agents, day	62 (14–240)
Total duration of use of anti-TNF agent, mo	56 (35–77)
Relapse during treatment	63 (37.9)
No. of relapses	
0	103 (62.1)
1	38 (23.9)
2	15 (9.0)
3	9 (5.4)
4	1 (0.6)
Final adult height Z-score	−0.17±0.96
Patients reaching MPH	90 (54.2)
Final adult height Z-score minus MPH Z-score	0.09±0.87

Data are presented as median (interquartile range), number (%), or mean±SD.
EEN, exclusive enteral nutrition; TNF, tumor necrosis factor; MPH, mid-parental height.

Table 3. Comparison between Patients Who Had and Had Not Reached MPH (n=166)

Variable	No (n=76)	Yes (n=90)	p-value
Male sex	49 (64.5)	62 (68.9)	0.662
Age at diagnosis, yr	15.0 (13.4–16.6)	14.9 (13.0–16.5)	0.673
IBD disease type			0.970
Crohn's disease	58 (76.3)	70 (77.8)	
Ulcerative colitis	18 (23.7)	20 (22.2)	
Family history of IBD	5 (6.6)	2 (2.2)	0.248
Height Z-score at diagnosis	–0.71±0.83	0.26±0.98	<0.001
Weight Z-score at diagnosis	–1.03±1.07	–0.50±1.30	0.005
BMI Z-score at diagnosis	–0.84 (–1.68 to –0.21)	–0.90 (–1.62 to 0.06)	0.720
MPH Z-score	–0.13±0.66	–0.39±0.68	0.015
Height Z-score at diagnosis minus expected final height Z-score	–0.65 (–1.04 to –0.27)	0.60 (0.17 to 1.08)	<0.001
Tanner stage 1–3	42 (55.3)	55 (61.1)	0.546
Moderate-to-severe disease at diagnosis	59 (77.6)	73 (81.1)	0.719
Baseline white blood cell count, /μL	9,465 (6,770–11,615)	9,340 (6,290–11,300)	0.808
Baseline Hematocrit, %	35.9±5.9	36.6 ± 4.9	0.404
Baseline Platelet, $\times 10^3/\mu L0$	424 (334–530)	416 (340–521)	0.852
Baseline Albumin, g/dL	3.8 (3.3–4.3)	3.9 (3.3–4.2)	0.880
Baseline erythrocyte sedimentation rate, mm/hr	39 (20–69)	44 (20–64)	0.955
Baseline C-reactive protein, mg/dL	3.30 (0.44–6.07)	2.64 (0.65–5.80)	0.885
Treatment with corticosteroids	26 (34.2)	39 (43.3)	0.298
Treatment with EEN	46 (62.2)	51 (58.0)	0.701
Treatment with immunomodulator	73 (96.1)	86 (95.6)	1.000
Treatment with anti-TNF agents	61 (80.3)	66 (73.3)	0.387
Duration from diagnosis to initiation of anti-TNF agents, day	60 (15 to 375)	64 (13 to 183)	0.441
Total duration of use of anti-TNF agent, mo	51 (27 to 74)	66 (37.5 to 84)	0.070
Relapse during treatment	26 (34.2)	37 (41.1)	0.452
Number of relapses	0 (0–1)	0 (0–1)	0.359
Final adult height Z-score	–0.77±0.70	0.33±0.85	<0.001
Final adult height Z-score minus MPH Z-score	–0.52 (–0.91 to –0.23)	0.58 (0.20 to 1.16)	<0.001

Data are presented as number (%), median (interquartile range), or mean±SD.
IBD, inflammatory bowel disease; BMI, body mass index; MPH, mid-parental height; EEN, exclusive enteral nutrition; TNF, tumor necrosis factor.

Table 4. Logistic Regression Analyses of Factors Associated with Reaching MPH (n=166)

	Univariate logistic regression analysis		Multivariate logistic regression analysis	
	OR (95% CI)	p-value	OR (95% CI)	p-value
Male sex	1.22 (0.64–2.34)	0.547		
Age at diagnosis	0.96 (0.83–1.11)	0.573		
IBD disease type–UC	0.92 (0.44–1.91)	0.823		
Height Z-score at diagnosis	3.22 (2.17–5.04)	<0.001	8.45 (4.44–17.90)	<0.001
Weight Z-score at diagnosis	1.46 (1.12–1.95)	0.006	0.91 (0.60–1.39)	0.663
BMI Z-score at diagnosis	1.07 (0.84–1.38)	0.584		
MPH Z-score	0.56 (0.34–0.89)	0.017	0.11 (0.04–0.24)	<0.001
Tanner stage 1–3	1.27 (0.68–2.37)	0.447		
Moderate-to-severe disease at diagnosis	1.24 (0.58–2.65)	0.580		
Treatment with corticosteroids	1.47 (0.79–2.78)	0.231		
Treatment with EEN	0.84 (0.44–1.58)	0.586		
Treatment with immunomodulator	0.88 (0.17–4.13)	0.874		
Treatment with anti-TNF agents	0.68 (0.32–1.40)	0.296		
Relapse during treatment	1.34 (0.71–2.54)	0.362		
Number of relapses	1.10 (0.79–1.57)	0.568		

MPH, mid-parental height; OR, odds ratio; CI, confidence interval; IBD, inflammatory bowel disease; UC, ulcerative colitis; BMI, body mass index; EEN, exclusive enteral nutrition; TNF, tumor necrosis factor.

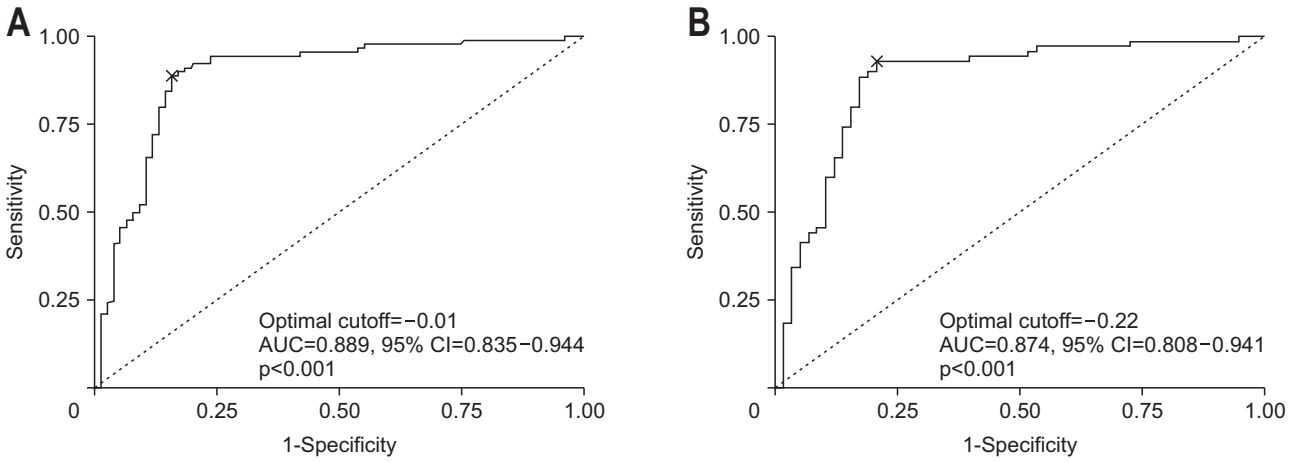

Fig. 1. Receiver operating characteristic curve of height Z-score at diagnosis minus mid-parenteral height Z-score for predicting reaching mid-parenteral height in (A) all included patients (n=166) and (B) patients with Crohn's disease (n=128). AUC, area under the curve; CI, confidence interval.

Table 5. Comparison between Patients Who Had and Had Not Reached Mid-Parental Adult Height among Crohn's Disease Patients (n=128)

Variable	No (n=58)	Yes (n=70)	p-value
Male sex	39 (67.2)	50 (71.4)	0.749
Age at diagnosis, yr	15.2 (13.7 to 16.6)	14.9 (13.0 to 16.5)	0.637
Family history of IBD	4 (6.9)	1 (1.4)	0.175
Height Z-score at diagnosis	−0.76±0.85	0.18±0.99	<0.001
Weight Z-score at diagnosis	−1.17±1.07	−0.66±1.17	0.012
BMI Z-score at diagnosis	−1.01±1.10	−0.92±1.21	0.681
MPH Z-score	−0.16±0.65	−0.38±0.72	0.071
Height Z-score at diagnosis minus expected final height Z-score	−0.65 (−1.06 to −0.29)	0.47 (0.08 to 0.97)	<0.001
Tanner stage 1–3	33 (56.9)	41 (58.6)	0.991
Any ileal involvement at diagnosis	53 (91.4)	61 (87.1)	0.631
Any colonic involvement at diagnosis	53 (91.4)	63 (90.0)	1.000
Any UGI tract involvement at diagnosis	36 (62.1)	44 (62.9)	1.000
B1 behavior at diagnosis	38 (65.5)	47 (67.1)	0.995
Perianal disease modifier at diagnosis	32 (55.2)	39 (55.7)	1.000
Baseline PCDAI	42.5 (32.5 to 47.5)	37.5 (30 to 45)	0.199
Baseline white blood cell count, /μL	9,520 (7,160 to 11,510)	9,460 (7,170 to 11,400)	0.895
Baseline hematocrit, %	36.8±5.3	36.8±4.2	0.246
Baseline platelet, $\times 10^3/\mu L$	431 (342 to 571)	431 (351 to 549)	0.582
Baseline albumin, g/dL	3.7±0.6	3.7±0.6	0.981
Baseline erythrocyte sedimentation rate, mm/hr	45 (27 to 80)	47 (31 to 76)	0.739
Baseline C-reactive protein, mg/dL	4.54 (1.20 to 7.52)	3.51 (1.68 to 6.56)	0.419
Baseline fecal calprotectin, mg/kg	1,731 (576 to 2,000)	904 (426 to 2,000)	0.176
Treatment with corticosteroids	16 (27.6)	22 (31.4)	0.780
Treatment with EEN	46 (79.3)	50 (71.4)	0.412
Treatment with immunomodulator	58 (100.0)	67 (95.7)	0.251
Treatment with anti-TNF agents	51 (87.9)	56 (80.0)	0.334
Relapse during treatment	19 (32.8)	30 (42.9)	0.323
No. of relapses	0 (0 to 1)	0 (0 to 1)	0.212
Final adult height Z-score	−0.82±0.72	0.27±0.87	<0.001
Final adult height Z-score minus MPH Z-score	−0.66±0.53	0.65±0.59	<0.001

Data are presented as number (%), median (interquartile range), or mean±SD.
IBD, inflammatory bowel disease; BMI, body mass index; MPH, mid-parental height; UGI, upper gastrointestinal; B1, nonstricturing nonpenetrating behavior; PCDAI, Pediatric Crohn's Disease Activity Index; EEN, exclusive enteral nutrition; TNF, tumor necrosis factor.

92.9%, specificity 79.3%, positive predictive value 84.4%, negative predictive value 90.2%, p<0.001) (Fig. 1B).

DISCUSSION

This is the first multicenter study to investigate the af-

Table 6. Logistic Regression Analyses of Factors Associated with Reaching MPH among Crohn's Disease Patients (n=128)

	Univariate logistic regression analysis		Multivariate logistic regression analysis	
	OR (95% CI)	p-value	OR (95% CI)	p-value
Male sex	1.22 (0.57–2.60)	0.609		
Age at diagnosis	0.95 (0.80–1.12)	0.542		
Height Z-score at diagnosis	3.07 (1.98–5.09)	<0.001	6.94 (3.49–15.66)	<0.001
Weight Z-score at diagnosis	1.50 (1.10–2.11)	0.014	0.93 (0.57–1.50)	0.752
BMI Z-score at diagnosis	1.07 (0.79–1.45)	0.678		
MPH Z-score	0.62 (0.36–1.04)	0.073	0.14 (0.05–0.34)	<0.001
Tanner stage 1–3	1.07 (0.53–2.17)	0.849		
Moderate-to-severe disease at diagnosis	0.73 (0.28–1.82)	0.512		
Any ileal involvement	0.64 (0.19–1.97)	0.447		
B1 behavior	1.08 (0.51–2.25)	0.846		
Perianal disease modifier	1.02 (0.51–2.06)	0.951		
Treatment with corticosteroids	1.20 (0.56–2.62)	0.636		
Treatment with EEN	0.65 (0.28–1.47)	0.307		
Treatment with anti-TNF agents	0.55 (0.19–1.43)	0.232		
Relapse during treatment	1.54 (0.75–3.21)	0.243		
Number of relapses	1.21 (0.81–1.85)	0.364		

MPH, mid-parental height; OR, odds ratio; CI, confidence interval; BMI, body mass index; B1, nonstricturing nonpenetrating behavior; EEN, exclusive enteral nutrition; TNF, tumor necrosis factor.

fecting factors for reaching final adult height based on parental heights in Korean pediatric IBD patients.

In this study, the median height Z-score at diagnosis and final adult height at follow-up were both below –1 standard deviation, showing no growth failure. Usually, the assessment of linear height growth in pediatric IBD patients utilizes a growth curve based on the height of the general population. However, this measure does not track individual growth patterns and their potential associated with the heritability of parental height. The MPH is defined as the average of the child's mother and father heights, while the target height is the child's gender-adjusted MPH. It is more appropriate to investigate whether the final adult height has reached the target MPH by examining the parental height of each patient, rather than checking the growth rate according to the height growth curve of the general population.

With MPH as the growth target, about 56% of the patients reached the goal, and 45% did not. Based on parental height, Sawczenko *et al.*[7] showed that 19% of case subjects achieved final height, and Lee *et al.*[14] reported that 37% of patients reached their target final adult height. Our results showed that more patients reached their target final adult height compared to previous studies.

Recently, the treatment goal has changed to mucosal healing, exclusive enteral nutrition has been implemented from the early stage of diagnosis, and the remission rate is increasing by reducing steroid usage due to the introduction of biological agents and active treatment such as top-down or accelerated step-up.[15-19] These recent aggressive treatments are thought to contribute to the reduction of growth impairments and normalization of growth. Several studies have reported the effects of therapeutic drugs on growth. Corticosteroids remain the main cause of medication-induced growth impairment and may contribute to growth failure, particularly when used during puberty.[6,20] Another study found that growth improvement was independent of reductions in corticosteroid dose.[1,21] Previous studies demonstrated that pediatric patients treated with exclusive enteral nutrition had better remission rates and improved growth status in patients with CD compared with corticosteroid.[22-25] Immunosuppressants are widely used as a treatment for IBD in children, but there are currently no long-term data reporting better growth outcomes when introduced immediately after diagnosis. A study of children with moderate to severe CD showed that infliximab treatment improved linear growth during the first year of regular infusion and could catch up with significant growth.[26] Clinical response was associated with improved linear growth, particularly when anti-tumor necrosis factor agents was started early after diagnosis, and may be associated with improved growth when used during early puberty.[26-30] Another intervention that could achieve normalization of growth was surgical resection. Previous studies have reported that resection of local CD in treatment-resistant children achieved clear follow-up growth within the next 6 months early in disease progression.[31] Another study showed that a history of IBD-related surgery did not significantly affect final height.[14] In this study, we could not confirm this because there were no patients who required surgical treatment. In our study, there was no difference between groups according to treatment. This suggests that

it is possible to reach a predicted adult height if inflammation is well controlled by selecting an appropriate drug and treating it according to the severity of each patient rather than using a specific drug to achieve height growth.

In the present study, when comparing the median MPH Z-score of the patients, the MPH of the growth-impaired patients was significantly higher than the MPH of the non-growth-impaired patients. In addition, height Z-score at diagnosis and MPH Z-score were the only factors associated with reaching MPH. Growth impairment is more common in CD patients than UC. Therefore, CD patients were investigated separately, and the results were consistent with the overall patient outcomes. Preliminary analyses of adult height in familial and twin studies in the general population have shown that there is a 76% to 90% heritability of growth patterns, with a genetic influence still highly likely in malnutrition conditions.[32-34] Lee *et al.*[14] reported that unaffected siblings of patients with growth impairment had shorter stature than siblings of patients with non-growth impairment. This finding supports a strong genetic predisposition for final height. Therefore, parental height may be a key factor in determining the final adult height of patients with pediatric IBD.

This study has some limitations. Although meaningful as a multicenter study, generalization is limited due to the small total number of patients. A second limitation is that we did not include bone age in the patient's growth assessment. Bone age is a definitive and objective indicator of growth retardation in childhood. Unfortunately, we were not able to measure it in this study. Finally, although this study included the stages of puberty in patients, the onset of puberty was not documented in most patients, so the effect of puberty on final height could not be compared.

In conclusion, parental height is the strongest determinant of reaching final adult height in children IBD and should be an integral part of the assessment of growth in children with IBD. In particular, in pediatric patients who present with a negative "height Z-score at diagnosis minus MPH Z-score," efforts should be made to restore growth with individual treatment with specific growth goals to raise the low height Z-score at the time of diagnosis to the MPH Z-score level.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

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AUTHOR CONTRIBUTIONS

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