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Initial Abdominal CT and Laboratory Findings Prior to Diagnosis of Crohn's Disease in Children

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Purpose: To identify initial abdominal computed tomography (CT) and laboratory findings prior to a diagnosis of Crohn's disease (CD) in children.

Materials and Methods: In this retrospective study, patients (≤18 year-old) who were diagnosed with CD from 2004 to 2019 and had abdominal CT just prior to being diagnosed with CD were included in the CD group. Patients (≤18 years old) who were diagnosed with infectious enterocolitis from 2018 to 2019 and had undergone CT prior to being diagnosed with enterocolitis were included as a control group. We assessed the diagnostic performances of initial CT and laboratory findings for the diagnosis of CD using logistic regression and the area under the curve (AUC).

Results: In total, 107 patients (50 CD patients, 57 control patients) were included, without an age difference between groups (median 13 years old vs. 11 years old, p=0.119). On univariate logistic regression analysis, multisegmental bowel involvement, mesenteric vessel engorgement, higher portal vein/aorta diameter ratio, longer liver longitudinal diameter, lower hemoglobin (≤12.5 g/dL), lower albumin (≤4 g/dL), and higher platelet (>320×10^3/μL) levels were significant factors for CD. On multivariate analysis, multisegmental bowel involvement [odds ratio (OR) 111.6, 95% confidence interval (CI) 4.778–2605.925] and lower albumin levels (OR 0.9, 95% CI 0.891–0.993) were significant factors. When these two features were combined, the AUC value was 0.985 with a sensitivity of 96% and specificity of 100% for differentiating CD.

Conclusion: Multisegmental bowel involvement on CT and decreased albumin levels can help differentiate CD from infectious enterocolitis in children prior to a definite diagnosis of CD.

Key Words: Crohn disease; child; adolescent; early diagnosis; tomography, X-ray computed

INTRODUCTION

Crohn's disease (CD) is a chronic granulomatous inflammatory disease of the gastrointestinal (GI) tract and is more prevalent in children between 15 and 25 years old than adults.[1] The incidence of CD in the United States is 4.56 per 100000 persons, with approximately 15%–25% of those patients first being affected by CD during childhood.[2] Recently, more and more pediatric patients have been diagnosed with CD.[3,4] CD shows a chronic and long-term clinical course that is characterized by periods of remission or relapse.[5] If diagnosis is delayed, various complications, such as stricture, fistula, abscess, or perforation, can occur.[6] Therefore, early and accurate diagnosis of CD in childhood is crucial to preventing and reducing the repercussions of disease progression.

CD is initially limited to the mucosa with neutrophilic cryptitis and shallow aphthous ulcers; however, as it progresses, trans-

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mural and extramural involvement occurs as superficial ulcerations extend into the deep bowel wall with fistula or sinus tracts. Skipped lesions are other specific findings of CD.[1,7,8] Known imaging features of CD on computed tomography (CT) and magnetic resonance imaging (MRI) include abnormal bowel wall thickening with hyperenhancement and mural stratification. Increased mesenteric vascularity (the comb sign), pericolic/perienteric fat strandings, and fibrofatty proliferation are also commonly observed.[9-11]

For definite diagnosis of CD, clinical assessments are made with endoscopy and radiologic examinations. The radiologic examination includes small bowel follow-through, ultrasonography (US), CT enterography, and MR enterography. Among these methods, CT and MR enterography are favored because they can be used to assess disease extent with intra- or extraluminal manifestations.[10] However, CT enterography is more limited than MR enterography, especially in children, because of ionizing radiation, poor soft-tissue contrast, and lack of real-time cinematic imaging. MR enterography is regarded as the first-line modality for diagnosing and following pediatric CD.[11,12] However, MR enterography cannot be readily or frequently suggested to children with nonspecific abdominal symptoms, because it requires young children to endure a large amount of oral contrast, long examination times, sedation, and higher costs. Therefore, in the emergency room or outpatient clinics, the first imaging study for patients with nonspecific abdominal symptoms who have not yet been diagnosed with CD is still conventional CT.

Differentiating infectious enterocolitis and CD on imaging before a confirmative diagnosis of CD is difficult. Even though CT is not standard work-up for children with suspected CD, many children with GI symptoms undergo CT scans unexpectedly, before the suspicion of CD. For pediatric radiologists, it is still challenging to identify which children need further work-up to screen for CD from conventional abdominal CT. In a previous study, attempts were made to utilize clinical symptoms to differentiate enterocolitis and CD prior to a diagnosis of CD.[13] However, there have been no reports on conventional CT features that can differentiate the two conditions. If such conventional CT features are found, they can be used to screen pediatric patients so that those who need further examinations, such as endoscopy or MR enterography, can undergo them without delay.

Therefore, the purpose of this study was to identify initial abdominal CT and laboratory findings that can indicate CD and differentiate CD from infectious enterocolitis prior to the diagnosis of pediatric CD.

MATERIALS AND METHODS

Subjects

The Institutional Review Board (IRB) of our institution approved this retrospective study, and the requirement for informed consent was waived (IRB No. 4-2020-0579). Pediatric patients (≤18 years old) who were diagnosed with CD from 2004 to 2019 and had undergone abdominal CT just prior to the diagnosis of CD were included in the CD group. Patients who had already been diagnosed or treated for CD before the CT scan were not included in this study. Patients (≤18 years old) who were diagnosed with infectious enterocolitis from 2018 to 2019 and had undergone CT prior to diagnosis were included in the control group. Pediatric gastroenterologists diagnosed CD based on clinical symptoms, laboratory, colonoscopy results, CT findings, and pathologic results. Pediatric gastroenterologists diagnosed infectious enterocolitis based on clinical symptoms, laboratory tests, CT findings, and clinical manifestations during follow-up. We excluded patients who did not have laboratory test results within 30 days of the CT examination, who underwent CT scans with oral contrast or without intravenous contrast enhancement, or who had a history of other GI tract diseases, including ulcerative colitis, Behcet's disease, or any surgical history concerning the GI tract.

Age, sex, height (cm), weight (kg), and body mass index (BMI, kg/m^2) with z-scores at the time of the CT examination were collected from electronic medical records. Clinical symptoms were reviewed if recorded in the medical records. Laboratory results within 30 days of the CT examination were evaluated. Data for white blood cell count (WBC, $\times 10^3/\mu L$), hemoglobin (g/dL), hematocrit (%), platelet ($\times 10^3/\mu L$), neutrophil (%), erythrocyte sedimentation rate (ESR, mm/hr), C-reactive protein (CRP, mg/L), and albumin (g/dL) levels were collected. When laboratory tests were repeated within 1 month, the initial laboratory results that presented with abdominal symptoms were recorded.

CT image analysis

Conventional abdominal CT scans were performed using one of two scanners (Sensation 64, Somatom Definition Flash; Siemens Medical Solutions, Forchheim, Germany, or Revolution EVO; GE Healthcare, Milwaukee, WI, USA). An intravenous contrast agent was administered and hepatic venous phase images were evaluated. One pediatric radiologist with 11 years of experience who was blinded to patient information evaluated the CT images using the picture archiving and communication system at our institution (Centricity; GE Healthcare).

For the qualitative analysis of CT features, multisegmental bowel involvement was recorded when the bowel wall was abnormally thickened with hyperenhancement alternatively along delineable bowel loops on CT (Fig. 1). Mesenteric vessel engorgement was recorded when engorged vessels demonstrated the comb sign. Inflamed bowel involvement at the appendix was assessed, if present. Lymph node enlargement was recorded when any mesenteric lymph node was larger than 1 cm in its short diameter. We also assessed the images for the presence of perianal soft tissue asymmetry and perianal abscess.

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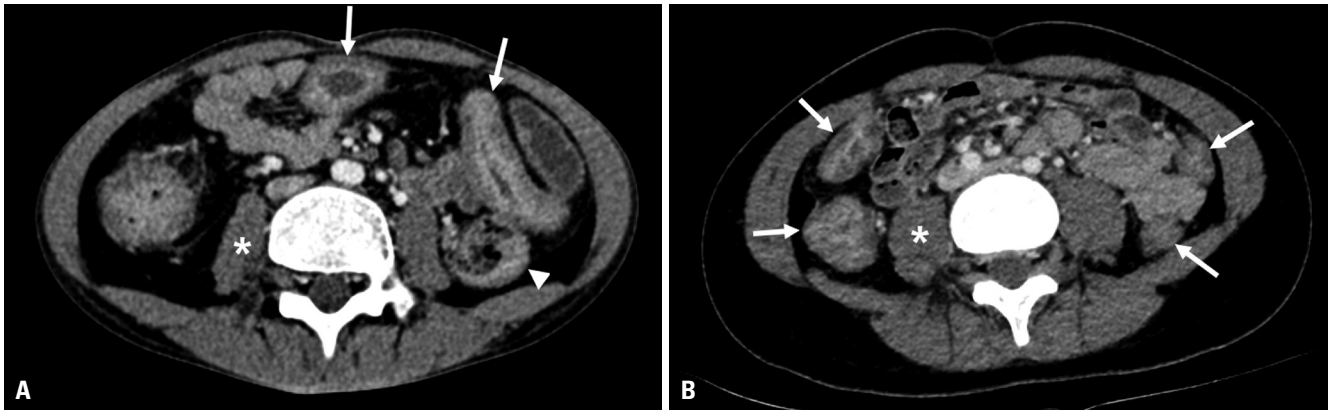

Fig. 1. Conventional abdominal CT images of patients with CD and infectious enterocolitis. (A) A 13-year-old boy was diagnosed with CD after this CT. Note multisegmental inflammation of ileal loops (arrows), compared with adjacent normal small bowel loops. Asymmetric wall thickening is also well noted at the descending colon (arrowhead). There was marked wall thickening at the ascending colon and relative thinning of the psoas muscle (asterisk). Initial laboratory results showed lower albumin levels (2.5 d/gL). (B) A 11-year-old girl was diagnosed with infectious enterocolitis after this CT. There was diffuse continuous inflammation of the colon (arrows) and a relatively thickened psoas muscle (asterisk). Her initial albumin level was 4.3 d/gL. CD, Crohn's disease.

For the quantitative analysis of CT features, the largest thickness of the small and large bowel wall (mm) was measured on axial images. For small bowel thickness, the small bowel loop among the duodenum, jejunum, and ileum that was the most thickened was selected for each patient and measured on an axial contrast-enhanced image. To understand the effects of sarcopenia, the thickness of the right psoas muscle (mm) at the level of aortic bifurcation was measured on an axial image (Fig. 1). The transverse diameters of the main portal vein and abdominal aorta (mm) at the same level of the liver hilum were used to evaluate differences in splanchnic vascular flow. The ratio between the portal vein and aorta diameter was evaluated to minimize the effect of patient size. In addition, the longitudinal diameter of the right liver lobe (cm) on coronal images was assessed for the presence of hepatomegaly.

Statistical analysis

Statistical analyses were performed using SPSS version 25 (IBM Corp., Armonk, NY, USA). Values were presented as medians with interquartile ranges or numbers with percentages. The Mann-Whitney U test was used for continuous variables and the chi-square test or Fisher's exact test was used for categorical variables.

A univariate logistic regression test was performed on features that were significantly different between the CD and control groups. Variables that did not occur in any of the two groups were not included in this analysis. For subsequent multivariate logistic regression analysis, five to seven variables were included with the overall subject number of this study following the rule of ten. Therefore, we could not include all of the variables that were significant on univariate analysis. Instead, we selected clinically accepted variables that are already known as meaningful features of CD or that had relatively consistent results without wide variation. In addition, for adjusting age, sex, and BMI z-score between two groups, a multivariate analysis was additionally performed that included these three variables. The diagnostic performances of significant variables for diagnosing CD were assessed using the area under the curve (AUC). *P*-values less than 0.05 were considered statistically significant.

RESULTS

Subjects and laboratory results

During the study period, 118 patients underwent abdominal CT scans before being diagnosed with CD or enterocolitis. Among these patients, eleven were excluded because laboratory results were unavailable within 30 days of the CT scan (n=3), oral contrast media was used (n=1), and a previous medical surgical history related to GI tract disease, including anorectal malformation or Behcet's disease, existed (n=7). Therefore, a total of 107 patients was included, with 50 patients in the CD group and 57 patients in the control group. Abdominal pain was present in 38 patients of the CD group and 51 patients in the control group. Diarrhea was present in 34 patients of the CD group and 19 patients in the control group. Weight loss occurred in 22 patients of the CD group, while only 2 patients had weight loss. The exact duration of abdominal pain, frequency of diarrhea, or extent of weight loss could not be confirmed when not recorded, especially for the control group, due to the retrospective study design. No one in the control group subsequently developed inflammatory bowel disease or other GI pathology during follow-up.

Basic patient demographics are compared between the CD and control groups in Table 1. Age, sex, height, and weight did not differ between the two groups (p=0.119, 0.174, 0.159, and 0.697, respectively). However, the z-scores of height and weight were significantly lower in the CD group (p=0.003, <0.001, respectively). BMI, BMI z-scores, and BMI percentage were also

Table 1. Comparison of Features between the CD and Control Groups

Variables	CD (n=50)	Control (n=57)	*p* value
Demographics			
Age (yr)	13 (11–14)	11 (10–14.5)	0.119
Sex (M:F)*	33:17	30:27	0.174
Height (cm)	155 (148–161.7)	150 (131.5–163.2)	0.159
Height z-core	-0.56 (-1.16–0.13)	0.3 (-0.62–0.99)	0.003
Weight (kg)	39 (31.3–49.8)	39 (30–52.9)	0.697
Weight z-score	-1.15 (-2.14– -0.3)	0.14 (-0.82–0.69)	<0.001
BMI (kg/m^2)	16.4 (14.5–19.2)	18.0 (15.6–21.2)	0.021
BMI z-score	-1.19 (-2.16– -0.07)	0.09 (-1.32–0.98)	0.001
BMI percentage (%)	19 (7–65)	54.5 (13.8–81.3)	0.029
Laboratory results			
WBC (×10^3/μL)	10125 (8207.5–12347.5)	6320 (5175–8960)	<0.001
Hemoglobin (g/dL)	11.6 (10.0–12.9)	13.4 (13.0–14.1)	<0.001
Hematocrit (%)	36.6 (32.5–39.5)	39.8 (37.5–41.9)	<0.001
Platelet (×10^3/μL)	517 (402–701.5)	266 (224.5–311.5)	<0.001
Neutrophil (%)	72.5 (66.5–79.2)	61 (47.9–76.9)	0.001
ESR (mm/hr)	73 (50–104)	3.5 (2–16.5)	<0.001
CRP (mg/L)	36 (11.7–75.8)	1.0 (0.3–20.2)	<0.001
Albumin (g/dL)	3.4 (3.1–3.7)	4.5 (4.3–4.7)	<0.001
Qualitative CT features			
Multisegmental bowel involvement	43 (86)	2 (3.5)	<0.001
Mesenteric vessel engorgement	41 (82)	2 (3.5)	<0.001
Appendix involvement*	7 (14)	0	0.004
Lymph node enlargement (short diameter >1 cm)	11 (22)	0	<0.001
Perianal soft tissue asymmetry	11 (22)	0	<0.001
Perianal abscess*	5 (10)	0	0.020
Quantitative CT features			
Largest thickness of the small bowel (mm)	7.5 (6.4–7.3)	6.2 (5.4–7.2)	<0.001
Largest thickness of the large bowel (mm)	10.2 (8.2–13.0)	10.3 (7–13.4)	0.937
Psoas muscle thickness (mm)	19.2 (15.3–24.4)	22 (17.6–27.1)	0.040
Portal vein (mm)	11.6 (10.1–12.8)	10.2 (9.1–11.4)	0.003
Abdominal aorta (mm)	13.4 (11.7–14.7)	13 (11.8–14.4)	0.844
Portal vein/aorta ratio	0.9 (0.8–1.0)	0.8 (0.7–0.9)	0.001
Liver longitudinal diameter (cm)	16.0 (15.1–17.4)	14.6 (13.6–15.3)	<0.001

CD, Crohn's disease; BMI, body mass index; WBC, white blood cell count; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein.
Data are presented as median (IQR) or n (%). The Mann-Whitney U test was performed for continuous variables, and the chi-square test (*Fisher's exact test) was performed for categorical variables.

all significantly lower in the CD group (p=0.021, 0.001, 0.029, respectively). All laboratory results were significantly different between the two groups. WBC (median 10125×10^3/μL vs. 6320×10^3/μL), platelet (median 517×10^3/μL vs. 266×10^3/μL), neutrophil (median 72.5% vs. 61%), ESR (median 73 mm/hr vs. 3.5 mm/hr), and CRP (median 36 mg/L vs.1.0 mg/L) levels were significantly higher in the CD group, while hemoglobin (median 11.6 g/dL vs. 13.4 g/dL), hematocrit (median 36.6% vs. 39.8%), and albumin (median 3.4 g/dL vs. 4.5 g/dL) levels were significantly lower in the CD group (all, p<0.001).

CT image results

In the qualitative analysis of CT features, multisegmental involvement (86% vs. 3.5%, p<0.001) and mesenteric vessel engorgement (82% vs. 3.5%, p<0.001) were observed significantly more in the CD group. No patient in the control group had appendix involvement, lymph node enlargement (short diameter >1 cm), perianal soft tissue asymmetry, or perianal abscess.

In the quantitative analysis of CT features, the largest thickness of the small bowel (median 7.5 mm vs. 6.2 mm, p<0.001), portal vein diameter (median 11.6 mm vs. 10.2 mm, p=0.003), portal vein/aorta ratio (median 0.9 vs. 0.8, p=0.001), and liver longitudinal diameter (median 16.0 cm vs. 14.6 cm, p<0.001)

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were significantly higher in the CD group. Psoas muscle thickness (median 19.2 mm vs. 22 mm, p=0.040) was significantly lower in the CD group. The largest thickness of the large bowel and abdominal aorta diameter did not differ between the CD and control group (Table 1).

Logistic regression results for differentiating CD

The results of univariate logistic regression analysis for differentiating CD from infectious enterocolitis are presented in Table 2. BMI z-score was a significant factor for predicting CD [odds ratio (OR) 0.708, 95% confidence interval (CI) 0.548–0.915]. Of the laboratory results, WBC (OR 1.0, 95% CI 1.000–1.000), hemoglobin (OR 0.4, 95% CI 0.275–0.587), hematocrit (OR 0.8, 95% CI 0.705–0.886), platelet (OR 1.0, 95% CI 1.008–1.019), neutrophil (OR 1.1, 95% CI 1.019–1.082), ESR (OR 1.1, 95% CI 1.044–1.125), CRP (OR 1.0, 95% CI 1.010–1.037), and albumin (OR 0.9, 95% CI 0.914–0.962) levels were significant factors for differentiating CD.

Table 2. Univariate Logistic Regression Analysis Results of Significant Features for Differentiating CD from Infectious Enterocolitis

Variables*	OR (95% CI)	p value
Demographics		
Age	1.072 (0.958–1.201)	0.226
Sex	0.572 (0.262–1.252)	0.162
Height	1.015 (0.995–1.035)	0.146
Height z-score	0.901 (0.761–1.067)	0.227
Weight	0.993 (0.968–1.018)	0.576
Weight z-score	0.645 (0.484–0.860)	0.003
BMI	0.891 (0.803–0.989)	0.030
BMI z-score	0.708 (0.548–0.915)	0.008
BMI percentage	0.986 (0.793–0.999)	0.034
Laboratory results		
WBC	1.000 (1.000–1.000)	0.001
Hemoglobin	0.402 (0.275–0.587)	<0.001
Hematocrit	0.790 (0.705–0.886)	<0.001
Platelet	1.014 (1.008–1.019)	<0.001
Neutrophil	1.050 (1.019–1.082)	<0.001
ESR	1.084 (1.044–1.125)	<0.001
CRP	1.023 (1.010–1.037)	<0.001
Albumin ($\times 10^2$)	0.938 (0.914–0.962)	<0.001
Qualitative CT features		
Multisegmental bowel involvement	168.929 (33.387–854.742)	<0.001
Mesenteric vessel engorgement	125.278 (25.685–611.049)	<0.001
Quantitative CT features		
Largest thickness of the small bowel	1.561 (1.214–2.008)	0.001
Psoas muscle thickness	0.948 (0.896–1.003)	0.062
Portal vein	1.372 (1.091–1.725)	0.007
Portal vein/aorta ratio ($\times 10$)	1.759 (1.244–2.487)	0.001
Liver longitudinal diameter	1.380 (1.112–1.713)	0.003

CD, Crohn's disease; OR, odds ratio; CI, confidence interval; BMI, body mass index; WBC, white blood cell count; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein.
*Except for variables without occurred events in the control group.

Of the CT features, multisegmental bowel involvement (OR 168.9, 95% CI 33.4–854.7), mesenteric vessel engorgement (OR 125.3, 95% CI 25.7–611.1), increase in the largest thickness of the small bowel (OR 1.6, 95% CI 1.214–2.008), portal vein diameter (OR 1.4, 95% CI 1.091–1.725), portal vein/aorta diameter ratio (OR 1.8, 95% CI 1.244–2.487), and liver longitudinal diameter (OR 1.4, 95% CI 1.112–1.713) were significant factors for differentiating CD. Age and psoas muscle thickness were not significant factors for CD (p=0.226 and p=0.062, respectively).

A maximum of seven variables among the above significant factors was allowed in the multivariate logistic regression analysis according to the rule of ten for the results to have clinical significance and consistency, and this judgement was made under the guidance of a statistician. We included multisegmental involvement, mesenteric vessel engorgement, portal vein/aorta diameter ratio, liver longitudinal diameter, and hemoglobin, platelet and albumin levels in the analysis, and the results are presented in Table 3. Of the seven variables, multisegmental involvement (OR 111.6, 95% CI 4.778–2605.925) and decreased albumin levels (OR 0.941, 95% CI 0.891–0.993) were significant factors for differentiating CD from infectious enterocolitis. For adjusting age, sex, and BMI z-score between the two groups, additional results including these three variables were also added to Table 3. Lower albumin level (OR 0.929, 95% CI 0.870–0.993) was a significant factor for predicting CD after adjusting for age, sex, and BMI z-score. Multisegmental bowel involvement showed a p-value of 0.086 after adjusting for age, sex, and BMI z-score.

Diagnostic performance for differentiating CD

When we assessed the diagnostic performances of significant variables for differentiating CD from infectious enterocolitis, as shown in Table 4, multisegmental involvement and higher platelet (>320×10^3/μL) and lower albumin (≤4 g/dL) levels showed AUC values above 0.9 for differentiating CD separately. Combining multisegmental involvement and lower albumin level together, the AUC value was 0.985 (95% CI 0.940–0.999) with a sensitivity of 96% and a specificity of 100% for differentiating CD from enterocolitis.

DISCUSSION

Cases of pediatric onset CD have gradually increased in number, and the timely recognition of CD in affected patients has become a critical issue.[3] About 15%–25% of patients who are newly diagnosed with inflammatory bowel disease are of the pediatric population, and reports have shown that CD patients are younger than patients with ulcerative colitis at the time of diagnosis.[14] CD has been characterized using CT or MRI be-

Table 3. Multivariate Logistic Regression Analysis Results of Significant Features for Differentiating CD from Infectious Enterocolitis, with or without Age, Sex, and BMI Adjustment

Variables*	OR (95% CI)	*p* value	OR (95% CI)	*p* value
Age	-	-	0.854 (0.308–2.368)	0.762
Sex	-	-	8.179 (0.019–3470.2)	0.496
BMI z-score	-	-	2.812 (0.349–22.662)	0.331
Hemoglobin	1.476 (0.379–5.751)	0.574	1.687 (0.289–9.842)	0.561
Platelet	1.002 (0.992–1.011)	0.729	1.008 (0.991–1.026)	0.349
Albumin ($\times 10^2$)	0.941 (0.891–0.993)	0.028	0.929 (0.870–0.993)	0.030
Multisegmental bowel involvement	111.587 (4.778–2605.925)	0.003	4416.306 (0.305–6397.9$\times 10^4$)	0.086
Mesenteric vessel engorgement	15.669 (0.159–1541.446)	0.240	69.617 (0.069–69816.414)	0.229
Portal vein/aorta ratio ($\times 10$)	1.462 (0.326–6.570)	0.620	1.249 (0.298–5.227)	0.761
Liver longitudinal diameter	1.565 (0.460–5.323)	0.473	1.726 (0.293–10.151)	0.546

CD, Crohn's disease; BMI, body mass index.
*Among the significant variables in Table 2, only variables that had clinical significance and relative consistency were included in the multivariate logistic regression analysis according to the rule of ten.

Table 4. Diagnostic Performance of Significant Features for Differentiating CD

Variables	Cut-off values	AUC	95% CI	Sensitivity (%)	Specificity (%)
Hemoglobin (g/dL)	≤12.5	0.843	0.760–0.906	72	87.7
Platelet ($\times 10^3$/μ L)	>320	0.940	0.877–0.977	96	80.7
Albumin (g/dL)	≤4	0.962	0.906–0.989	90	94.7
Multisegmental bowel involvement	-	0.912	0.842–0.958	86	94.5
Mesenteric vessel engorgement	-	0.892	0.818–0.944	82	96.5
Portal vein/aorta ratio	0.86	0.681	0.583–0.767	54	79.0
Liver longitudinal diameter (cm)	>15.3	0.708	0.612–0.792	68	77.2
Multisegmental bowel involvement+Albumin	-	0.985	0.940–0.999	96	100

CD, Crohn's disease; AUC, area under the curve; CI, confidence interval.

cause active inflammation of the bowel loop on histology is a well-known trait of CD in pediatric patients.[12] However, it is not easy to differentiate CD from enterocolitis with conventional abdominal CT. Abdominal pain and GI symptoms may be early presentations of CD, and a faster diagnosis of CD could lead to fewer affected bowel loops than would be expected with disease progression. However, differentiating CD from other enterocolitis using conventional CT, as is done in the emergency department, can be challenging without CT or MR enterography.

A recent study mentioned that even clinicians in a tertiary hospital rarely encounter CD in its early stages before complications arise, such as fistula or abscess.[6] Kwon, et al.[13] demonstrated that body mass index and initial basic laboratory results, including WBC, hemoglobin, and serum albumin levels, were significantly lower in CD than in ulcerative colitis before a final diagnosis of inflammatory bowel disease. Irwin, et al.[15] proved that serum albumin significantly decreased and serum platelet significantly increased during follow-up in a CD group before final diagnosis. These findings emphasize the need to detect pre-diagnosis symptoms and signs to reduce diagnostic lag times and delays in treatment access.[15]

To the best of our knowledge, we are the first to analyze routine abdominal CT findings in qualitative and quantitative ways to detect pre-diagnostic changes on the CT images of CD patients. Even though we could not include all of the variables that were significant on univariate analysis in the multivariate regression analysis, we were able to demonstrate that many laboratory and CT findings can aid the differentiation of CD from infectious enterocolitis as was also seen with the results of the univariate regression test. In addition to already known CT findings of CD, such as multisegmental involvement and the comb sign, we attempted to quantify sarcopenia and splanchnic vasculature using psoas muscle thickness and portal vein/aorta ratio despite the limitations of using such features. In multivariate analysis, multisegmental bowel involvement on initial CT and lower serum albumin levels (≤4 g/dL) showed an AUC value of 0.985 with a sensitivity of 96% and a specificity of 100%. This result was concordant with a previous study that concentrated on laboratory results obtained before a CD diagnosis.[13,15] Even though routine pediatric abdominal CT without oral contrast media or multiphase scanning does not fully demonstrate and characterize the bowel loop, compared with CT or MR enterography, efforts to simply trace the inflamed bowel segment and refer to laboratory results could effectively help clinicians and radiologists identify patients who need further work-up.

Sarcopenia due to malnutrition has emerged as an important problem for CD patients.[16-18] There have been efforts made

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to quantify the body composition of CD patients using the psoas muscle area on routine MRI.[19] In our study, psoas muscle thickness was significantly lower in CD patients on initial abdominal CT (19.2 mm vs. 22 mm, p=0.040). This suggests that sarcopenia can be observed in the initial presentation of CD and can worsen as CD progresses, although further studies are needed to confirm this assumption. Some studies have raised concerns that CD patients might have increased splanchnic vascular flow seen on Doppler US or contrast-enhanced US.[20,21] Our study showed that while aorta diameter was not significantly different, portal vein diameter and the ratio between the two diameters were significantly larger in the CD group. Further studies with a larger pediatric cohort that focus on splanchnic perfusion and its effect on the abdominal organs or liver are warranted.

Our study has several limitations. First, because of its retrospective nature, a selection bias could exist. In addition, we could not include all of the significant variables in the multivariate analysis because the small number of included subjects became the cause of failure of assumption. We had to select a maximum of seven variables with clinical importance and narrowed variation following the rule of ten. Additionally, we included age, sex, and BMI in the selected seven variables to show results after adjusting clinical factors of two groups. Second, one pediatric radiologist assessed CT features without demonstrating inter- or intra-observer variability. However, most of the features included in this study were not measured with new techniques, and we tried to include features that would be less affected by measurements. Future large cohort studies in real clinical settings are needed to validate our results.

In conclusion, initial conventional CT and laboratory results could aid in the differentiation of CD from infectious enterocolitis prior to the diagnosis of CD in pediatric patients. Detection of multisegmental bowel involvement on initial CT and lower albumen levels (≤4 g/dL) could aid the differentiation of CD from enterocolitis. Even though routine pediatric abdominal CT without oral contrast or multiphase scanning does not fully demonstrate and characterize the bowel loop, compared with CT or MR enterography, efforts to simply trace the inflamed bowel segment while referring to laboratory results could effectively help clinicians and radiologists identify patients who need further work-up.

AUTHOR CONTRIBUTIONS

Conceptualization: Hyun Joo Shin, Mi-Jung Lee, Haesung Yoon, Hong Koh, Seung Kim, and Sowon Park. Data curation: Choeum Kang and Hyun Joo Shin. Formal analysis: Hyun Joo Shin and Kyunghwa Han. Investigation: Choeum Kang, Kyunghwa Han, and Hyun Joo Shin. Methodology: Hyun Joo Shin and Kyunghwa Han. Project administration: Hyun Joo Shin, Hong Koh, Mi-Jung Lee, Sowon Park, Seung Kim, and Haesung Yoon. Resources: Hyun Joo Shin, Choeum Kang, Hong Koh, Mi-Jung Lee, Sowon Park, Seung Kim, and Haesung Yoon. Software: Hyun Joo Shin and Choeum Kang. Supervision: Hyun Joo Shin, Kyunghwa Han, Sowon Park, Seung Kim, Hong Koh, Mi-Jung Lee, Haesung Yoon, and Jisoo Kim. Validation: Choeum Kang and Hyun Joo Shin. Visualization: Choeum Kang and Hyun Joo Shin. Writing—original draft: Hyun Joo Shin and Choeum Kang. Writing—review & editing: Hyun Joo Shin, Choeum Kang, and Kyunghwa Han. Approval of final manuscript: all authors.

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REFERENCES

1. Gore RM, Levine MS. Textbook of gastrointestinal radiology. 2nd ed. Philadelphia: W.B. Saunders; 2000.
2. Kim SC, Ferry GD. Inflammatory bowel diseases in pediatric and adolescent patients: clinical, therapeutic, and psychosocial considerations. Gastroenterology 2004;126:1550-60.
3. Sýkora J, Pomahačová R, Kreslová M, Cvalínová D, Štych P, Schwarz J. Current global trends in the incidence of pediatric-onset inflammatory bowel disease. World J Gastroenterol 2018;24:2741-63.
4. Benchimol EI, Fortinsky KJ, Gozdyra P, Van den Heuvel M, Van Limbergen J, Griffiths AM. Epidemiology of pediatric inflammatory bowel disease: a systematic review of international trends. Inflamm Bowel Dis 2011;17:423-39.
5. Kim HJ, Kim Y, Cho JM, Oh SH, Kim KM. Therapeutic efficacy of oral enteral nutrition in pediatric Crohn's disease: a single center non-comparative retrospective study. Yonsei Med J 2016;57:1185-91.
6. Freeman HJ. Natural history and long-term clinical course of Crohn's disease. World J Gastroenterol 2014;20:31-6.
7. Gore RM, Balthazar EJ, Ghahremani GG, Miller FH. CT features of ulcerative colitis and Crohn's disease. AJR Am J Roentgenol 1996;167:3-15.
8. Furukawa A, Saotome T, Yamasaki M, Maeda K, Nitta N, Takahashi M, et al. Cross-sectional imaging in Crohn disease. Radiographics 2004;24:689-702.
9. Toma P, Granata C, Magnano G, Barabino A. CT and MRI of paediatric Crohn disease. Pediatr Radiol 2007;37:1083-92.
10. Dillman JR, Adler J, Zimmermann EM, Strouse PJ. CT enterography of pediatric Crohn disease. Pediatr Radiol 2010;40:97-105.
11. Chalian M, Ozturk A, Oliva-Hemker M, Pryde S, Huisman TA. MR enterography findings of inflammatory bowel disease in pediatric patients. AJR Am J Roentgenol 2011;196:W810-6.
12. Gale HI, Sharatz SM, Taphey M, Bradley WF, Nimkin K, Gee MS. Comparison of CT enterography and MR enterography imaging features of active Crohn disease in children and adolescents. Pediatr Radiol 2017;47:1321-8.
13. Kwon YH, Kim YJ. Pre-diagnostic clinical presentations and medical history prior to the diagnosis of inflammatory bowel disease in children. Pediatr Gastroenterol Hepatol Nutr 2013;16:178-84.
14. Heikenen JB, Werlin SL, Brown CW, Balint JP. Presenting symptoms and diagnostic lag in children with inflammatory bowel disease. Inflamm Bowel Dis 1999;5:158-60.
15. Irwin JR, Ferguson E, Simms LA, Hanigan K, Doecke JD, Lang-

guth D, et al. Detectable laboratory abnormality is present up to 12 months prior to diagnosis in patients with Crohn's disease. Dig Dis Sci 2019;64:503-17.
16. Palmese F, Del Toro R, Di Marzio G, Cataleta P, Sama MG, Domenicali M. Sarcopenia and vitamin D deficiency in patients with Crohn's disease: pathological conditions that should be linked together. Nutrients 2021;13:1378.
17. Dhaliwal A, Quinlan JI, Overthrow K, Greig C, Lord JM, Armstrong MJ, et al. Sarcopenia in inflammatory bowel disease: a narrative overview. Nutrients 2021;13:656.
18. Atlan L, Cohen S, Shiran S, Sira LB, Pratt LT, Yerushalmy-Feler A. Sarcopenia is a predictor for adverse clinical outcome in pediatric inflammatory bowel disease. J Pediatr Gastroenterol Nutr 2021; 72:883-8.
19. Ashton JJ, Peiris D, Green Z, Johnson MJ, Marino LV, Griffiths M, et al. Routine abdominal magnetic resonance imaging can determine psoas muscle area in paediatric Crohn's disease and correlates with bioelectrical impedance spectroscopy measures of lean mass. Clin Nutr ESPEN 2021;42:233-8.
20. Andrade TG, Fogaça HS, Elia CC, Pitrowsky MT, Souza HS. Crohn's disease activity assessed by Doppler sonography: the role of aortic flow parameters. Clinics (Sao Paulo) 2013;68:457-62.
21. Maconi G, Asthana AK, Bolzacchini E, Dell'Era A, Furfaro F, Bezzio C, et al. Splanchnic hemodynamics and intestinal vascularity in Crohn's disease: an in vivo evaluation using Doppler and contrast-enhanced ultrasound and biochemical parameters. Ultrasound Med Biol 2016;42:150-8.

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