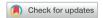


Original Article





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Conflict of Interest

The authors have no financial conflicts of interest.

ABSTRACT

Purpose: The clinical implications of bowel wall thickening (BWT) on abdominal computed tomography (CT) among children are unknown. We aimed to suggest a new method for measuring BWT and determining its clinical significance in children.

Methods: We retrospectively analyzed 423 patients with acute abdomen who underwent abdominal CT; 262 were classified into the BWT group. For this group, the pediatric radiologist described the maximal bowel wall thickness (MT), normal bowel wall thickness (mm) (NT), and their ratios for each segment of the bowel wall.

Results: In the thickened bowel walls, the thickness differed significantly between the small bowel (6.83±2.14 mm; mean±standard deviation) and the colon (8.56±3.46 mm; *p*<0.001). The ratios of MT to NT in the small bowel (6.09±3.17) and the colon (7.58±3.70) were also significantly different (*p*<0.001). In the BWT group, 35 of 53 patients had positive fecal polymerase chain reaction results; 6 patients infected with viruses predominantly had BWT in the small intestine, while the terminal ileum and the colon were predominantly affected in 29 patients with bacterial infections. In the initially undiagnosed 158 patients with BWT, the symptoms improved spontaneously without progression to chronic gastrointestinal disease. Conclusion: This study provides a clinical reference value for BWT in the small intestine and colon using a new method in children. The BWT on abdominal CT in children might indicate nonspecific findings that can be observed and followed up without additional evaluation, unlike in adults.

Keywords: Bowel wall thickening; Abdominal pain; Multidetector computed tomography; Child

INTRODUCTION

The use of abdominal computed tomography (CT) for evaluating pediatric abdominal pain has markedly increased over the past decades due to its improved diagnostic accuracy, leading to increased sensitivity and specificity [1]. Bowel wall thickening (BWT) is not an uncommon abdominal CT finding in pediatric patients. However, there is no clear guideline or consensus regarding the appropriate method for measuring bowel wall thickness or determining its clinical management [2].

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BWT observed on abdominal CT may be caused by several pathological conditions, including infection, hemorrhage, and neoplastic disease. However, it may also be a normal variant [3]. Previous adult studies have strongly recommended further endoscopic investigation for BWT because most could have a significant disease, such as malignancy [4,5]. However, because of the low risk of intestinal malignancy in children, a different approach for the evaluation and subsequent clinical management of BWT is needed. There are insufficient studies in the pediatric age group regarding the proper approach to BWT and its relation to significant disease.

The normal and abnormal thickness of the bowel wall can vary significantly depending on the degree of bowel distension. A distended bowel can lead to a thinner than normal wall [6]. Furthermore, BWT may be erroneously reported as abnormal on CT in cases of bowel collapse or partial distension. It may also be challenging to determine due to fluid, fecal contents, or redundant bowel [7]. Therefore, it is difficult to define the reference value of bowel wall thickness, especially in children. Some researchers have used a measurement of 2-3 mm as the upper limit of normal bowel wall thickness, while others have suggested that the presence of any perceptible thickening is abnormal [3]. However, all these reports were for adults, and no studies have provided a pediatric reference value for determining BWT.

This study's primary objective was to present a novel measurement method and clinical reference values for BWT using abdominal CT among children. The secondary objective was to determine the clinical significance of BWT in symptomatic children with no history of gastrointestinal disease.

MATERIALS AND METHODS

Study design and subjects

We retrospectively reviewed the medical records of patients aged <18 years who underwent abdominal CT for the evaluation of acute abdomen between July 2015 and December 2016 at a tertiary medical center. We excluded patients with underlying chronic diseases, such as inflammatory bowel disease, malignancy, chronic kidney disease, gynecologic disease, and those with diagnoses other than gastrointestinal diseases, including kidney disease, gynecologic disease, and musculoskeletal disease based on abdominal CT. This study was approved by the Institutional Review Board of Ewha Womans University Medical Center (EUMC 2016-10-045-001).

The following data were collected: patient's age, sex, and anthropometric measurements; clinical symptoms, including fever, abdominal pain, vomiting, diarrhea, and hematochezia; abdominal physical examination, laboratory, and abdominal CT findings; and the final diagnosis. To detect pathogens in the fecal samples, a multiplex real-time polymerase chain reaction (PCR) assay (Seeplex® Diarrhea ACE detection kits; Seegene, Seoul, Korea) was used for viruses, including group A rotavirus, norovirus, enteric adenovirus, and astrovirus, and bacteria, including Vibrio spp., Salmonella spp., Campylobacter spp., Yersinia enterocolitica, and verotoxigenic Escherichia coli.

The patients were then divided into two groups: those with BWT on abdominal CT (the BWT group) and those with no BWT on abdominal CT (the non-BWT group). Medical records were reviewed by two pediatricians who were blinded to the final diagnosis.

Method for measuring bowel wall thickness

Abdominal CT with intravenous contrast was performed using a 16- or 64-slice CT scanner (SOMATOM, Sensation 16 or 64; Siemens Medical Solutions, Erlangen, Germany). We reviewed the medical records of patients with BWT on abdominal CT. No strict definition of BWT exists in the literature; thus, the description was based on the radiologist's interpretation of the CT report. Our initial search yielded 450 patients, with 423 meeting the study's inclusion criteria. For the patients identified with BWT in the initial search, a pediatric radiologist blinded to the clinical diagnosis described the maximal bowel wall thickness (mm) (MT) at the segment of BWT and the normal bowel wall thickness (mm) (NT) adjacent to the BWT segment specifically for each segment, including the duodenum, jejunum, ileum, terminal ileum, cecum, ascending colon, transverse colon, descending colon, and rectosigmoid colon. The ratios of MT to NT (MT/NT ratios) were determined for each bowel wall segment.

Follow-up in the undiagnosed bowel wall thickening group

We reviewed the medical records on follow-up abdominal ultrasonography performed after a few months in the BWT group for pediatric out-patient department (OPD). Patients in the BWT group who did not undergo follow-up abdominal ultrasonography due to spontaneous recovery or mild symptoms were followed up at the OPD. Patients who did not visit the OPD clinic were followed up by telephone.

Statistics

Data were analyzed using IBM SPSS Statistics, version 20.0 (IBM Co., Armonk, NY, USA). The thickness (mm) of the bowel wall and the MT/NT ratios are expressed as the mean, standard deviation, and median (interquartile range [IQR]) because the variables were non-normally distributed. Categorical variables were analyzed using Pearson's chi-square test and Fisher's exact test, and continuous variables were analyzed using the Mann-Whitney U-test. Statistical significance was defined as p < 0.05.

RESULTS

Patient characteristics

A total of 423 patients were enrolled in this study, including 262 (median [IQR]: 10.6 years [7.6–13.7], male 53.8%) in the BWT group and 161 (median [IQR]: 10.3 [6.0–13.5], male 49.1%) in the non-BWT group (**Table 1**). Of these patients, 61.8% showed BWT on abdominal CT. No significant differences were found between the BWT and non-BWT groups (p>0.05) in terms of age, sex, clinical symptoms (fever, abdominal pain, and vomiting), physical examination results, and laboratory findings (hematocrit and albumin) (**Table 1**). However, there were significant differences in the duration and frequency of diarrhea and the serologic inflammatory markers, including leukocytes, neutrophils, and C-reactive protein (p<0.05) (**Table 1**).

In the BWT group, 104 patients were diagnosed with the following conditions based on the abdominal CT, clinical symptoms, or endoscopic findings (**Table 2**): 94 cases of acute appendicitis (35.9%), 4 cases of intussusception (1.5%), 3 cases of inflammatory bowel diseases (1.1%), 2 cases of diverticulitis (0.8%), and 1 case of hemorrhagic colitis (0.4%). Of the 158 patients who were initially undiagnosed, 94 were classified into the gastroenteritis group based on their diarrhea symptoms or positive fecal PCR findings irrespective of

Table 1. The characteristics of patients with or without BWT on abdominal computed tomography

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Characteristic	BWT group (n=262)	Non-BWT group (n=161)	
Age (y)	10.6 (7.6-13.7)	10.3 (6.0-13.5)	
Male	141 (53.8)	79 (49.1)	
Clinical symptom			
Fever (d)	2 (1-3)	2 (1–3)	
Abdominal pain (d)	2 (1-3)	2 (1–3)	
Diarrhea*	116 (44.3)	35 (21.7)	
Duration (>5 d)*	16 (6.1)	2 (1.2)	
Frequency (>4/d)*	45 (17.2)	6 (3.7)	
Vomiting	102 (38.9)	54 (33.5)	
Duration (>2 d)	24 (9.2)	21 (13.0)	
Frequency (>2/d)	68 (26.0)	41 (25.5)	
Physical examination			
Direct tenderness	242 (92.4)	144 (89.4)	
Rebound tenderness	38 (14.5)	14 (8.7)	
Laboratory finding			
Hematocrit (%)	37.9 (35.9-40.1)	38.4 (36.0-40.0)	
Leukocyte (/mm³)*	11,245 (8,020-15,187.5)	9,160 (6,735-12,472.5)	
Neutrophil (%)*	76.1 (65.7-83.4)	64.4 (50.3-76.6)	
Albumin (g/dL)	4.2 (4.0-4.4)	4.2 (4.0-4.4)	
C-reactive protein (mg/dL)	1.86 (0.32-6.05)	0.21 (0.04-0.91)	

Values are presented as median (interquartile range) or number (%).

diarrhea symptoms (**Table 2**). Meanwhile, 64 patients who had abdominal pain without diarrhea, negative fecal PCR findings, or no fecal PCR assay performed were classified into the nonspecific group (**Table 2**).

Among the 161 patients in the non-BWT group, there were 8 cases of intussusception (5.0%), 2 cases of intestinal malrotations (1.2%), and 1 case each of intraperitoneal abscess (0.6%), acute pancreatitis (0.6%), Meckel's diverticulitis (0.6%), and mesenteric panniculitis (0.6%) based on the abdominal CT findings. In addition, 36 patients (22.4%) in the non-BWT group

Table 2. The diagnosis of patients with or without BWT on abdominal computed tomography

Diagnosis	BWT group	Non-BWT group
Diagnosed group	104 (39.7)	14 (8.7)
Acute appendicitis	94 (35.9)	0 (0.0)
Intussusception	4 (1.5)	8 (5.0)
Inflammatory bowel disease	3 (1.1)	0 (0.0)
Crohn's disease	2 (0.8)	0 (0.0)
Ulcerative colitis	1 (0.4)	0 (0.0)
Diverticulitis	2 (0.8)	0 (0.0)
Intestinal malrotation	0 (0.0)	2 (1.2)
Hemorrhagic colitis	1 (0.4)	0 (0.0)
Intra-abdominal abscess	0 (0.0)	1 (0.6)
Acute pancreatitis	0 (0.0)	1 (0.6)
Meckel's diverticulitis	0 (0.0)	1 (0.6)
Mesenteric panniculitis	0 (0.0)	1 (0.6)
Undiagnosed group	158 (60.3)	147 (91.3)
Gastroenteritis	94 (35.9)	36 (22.4)
Stool PCR positive	34 (13.0)	6 (3.7)
Stool PCR negative	13 (5.0)	4 (2.5)
Stool PCR not done	47 (17.9)	26 (16.1)
Nonspecific	64 (24.4)	111 (68.9)
Total	262 (100)	161 (100)

Values are presented as a number (%).

BWT: bowel wall thickening, PCR: polymerase chain reaction.

BWT: bowel wall thickening.

^{*}p<0.05.



were diagnosed with gastroenteritis; of these, positive PCR findings were found in 6, negative PCR findings were found in 4, and the remaining 26 patients did not undergo PCR assays.

Clinical reference values for bowel wall thickening

The MT, NT, and MT/NT ratios were described from the 158 patients initially undiagnosed in the BWT group. Among the 262 patients with a clear diagnosis, 104 were excluded. The segment in which BWT was most frequently found on abdominal CT was the terminal ileum (38.2%), while it was least frequently found in the duodenum (1.1%) (**Table 3**). In the normal bowel wall, the thickness was not significantly different from the duodenum to the rectosigmoid segment or between the small bowel and the colon (p>0.05) (**Table 3**). In the BWT segment, the thickness significantly differed between the small bowel (6.83 \pm 2.14 [6.70] mm), and the colon (8.56 \pm 3.46 [7.90] mm; p<0.001) (**Table 3**). The jejunum showed a minimum thickness of 5.43 \pm 2.05 (4.90) mm, and the ascending colon showed a maximum thickness of 10.32 \pm 3.75 (9.60) mm (**Table 3**). The MT/NT ratios of the small bowel and colon were significantly different (p<0.001) (**Table 3**). In the jejunum, the reference values of MT/NT ratios were the lowest (4.01 \pm 1.30 [4.03] mm), while these were highest (8.95 \pm 4.26 [8.19] mm) in the ascending colon (**Table 3**).

Pathogens detected with fecal polymerase chain reaction assay associated with the bowel wall thickening group

In the BWT group, 53 patients underwent fecal PCR assays (**Fig. 1**). Among them, 35 (66.0%) had positive fecal PCR results, with viruses and bacteria being detected in six and 29 patients, respectively (**Fig. 1**). Specifically, the detected viruses included *norovirus* (3/6), *rotavirus* (2/6), and *astrovirus* (1/6), while the bacteria detected were *Campylobacter* (20/29), *Salmonella* (7/29), *Yersinia* (1/29), and verotoxigenic *Escherichia coli* (1/29). *Norovirus* and *Campylobacter* were simultaneously detected in one patient (**Fig. 1**). In the non-BWT group, 14 patients underwent

Table 3. Measured values of bowel wall thickness on abdominal computed tomography

Location	N	Normal bowel wall (mm)	Thickened bowel wall (mm)	Ratio (thickened/normal)
Small bowel				
Duodenum	3	1.10±0.17	6.77±2.50	6.04±1.54
		1.20 (0.90-)	6.70 (4.30-)	5.58 (4.78-)
Jejunum	10	1.40±0.43	5.43±2.05	4.01±1.30
		1.30 (1.05-1.85)	4.90 (3.50-6.88)	4.03 (2.77-4.79)
Ileum	8	1.31±0.50	6.44±1.37	5.45±1.97
		1.30 (0.83-1.80)	6.00 (5.30-7.48)	4.81 (4.02-7.59)
Terminal ileum	100	1.38±1.02	7.00±2.17	6.35±3.34
		1.20 (0.90-1.60)	7.00 (5.60-8.48)	5.74 (4.21-7.40)
Entire small bowel	121	1.37±0.94	6.83±2.14	6.09±3.17
		1.20 (0.90-1.60)	6.70 (5.40-8.30)	5.35 (4.08-7.20)
Colon				
Cecum	32	1.25±0.37	10.16±3.30	8.72±3.47
		1.20 (1.00-1.58)	9.80 (7.38-12.00)	7.79 (5.61–12.00)
Ascending colon	81	1.25±0.45	10.32±3.75	8.95±4.26
		1.20 (0.90-1.60)	9.60 (7.95-12.65)	8.19 (6.28-10.00)
Transverse colon	60	1.17±0.40	7.46±2.73	6.85±2.84
		1.10 (0.93-1.38)	7.10 (5.43-9.00)	6.49 (4.64-8.30)
Descending colon	44	1.23±0.44	6.66±2.04	6.08±3.08
		1.15 (0.90-1.60)	6.20 (5.30-7.68)	5.66 (4.10-7.38)
Recto-sigmoid colon	20	1.23±0.41	6.31±1.90	5.68±2.46
		1.20 (0.90-1.65)	5.65 (5.20-7.45)	4.71 (4.02-8.22)
Entire colon	237	1.23±0.42	8.56±3.46	7.58±3.70
		1.20 (0.90-1.60)	7.90 (6.00-10.45)*	7.00 (5.07-9.00)*

Values are presented as mean±standard deviation and median (interquartile range).

^{*}p<0.001 vs. entire small bowel.

(s) Salmonella

(a) Astrovirus

© Campylobacter (V) VTEC (n) Norovirus (y) Yersinia (r) Rotavirus Virus Positive rate (a) (r) (r) (r) (a) (r) (11/61)(n)-(c) (n)(n)(n)(n) **BWT** SB TI+colon Colon None SB+colon (0)(0)(0)(0) (C)Bacteria (0)(0)(0)(c)(c)(c)(c)(n)-(c) **\$**\$\$\$\$ Positive rate (30/62)(y) (s) (s) (v)

Fig. 1. Distribution of bowel wall thickening according to the stool pathogens detected with polymerase chain reaction assay.

VTEC: verotoxigenic Escherichia coli, BWT: bowel wall thickening, SB: small bowel, TI: terminal ileum.

fecal PCR. Among them, six (42.9%) tested positive for *rotavirus* (2/5), *norovirus* (2/5), *astrovirus* (1/5), and *Campylobacter* (1) (**Fig. 1**).

Distribution of bowel wall thickening according to the pathogens

Among the 11 patients detected with a viral infection by the fecal PCR assay, BWT was absent in 5 patients (45.5%), but the remaining were observed with small bowel BWT (3 cases), terminal ileum and colonic BWT (2 cases), and colonic BWT (1 case) (Fig. 1). In comparison, 93.3% of the patients (28/30) with positive bacterial infection of fecal PCR showed BWT in the terminal ileum and colon. However, one patient infected with *Salmonella* showed BWT in the small bowel and colon, and another patient infected with *Campylobacter* showed no BWT on abdominal CT (Fig. 1). According to the pathogens identified by fecal PCR, BWT was mainly distributed in the small intestine in patients with viral infections and the terminal ileum and colon in patients with bacterial infections (Fig. 1).

Follow-up in the undiagnosed bowel wall thickening group

In the undiagnosed BWT group, six out of 94 patients in the gastroenteritis group underwent abdominal ultrasonography between 4 and 4.5 months (median 3.25 months) after abdominal CT examination and showed no BWT findings. The other 88 patients in the gastroenteritis group did not require follow-up abdominal ultrasonography because they improved spontaneously and did not progress to chronic intestinal disease. Meanwhile, among the 64 patients in the non-gastroenteritis group, we confirmed the spontaneous recovery of acute abdominal pain and non-progression to chronic gastrointestinal disease between 4.5 months and 16 months after abdominal CT evaluation using medical records for six patients and by telephone follow-up for 30 patients. The remaining 28 patients were lost to follow-up.

DISCUSSION

In this study, the MT/NT ratios on abdominal CT of the intestinal segment in each patient were presented as a novel method for measuring BWT in pediatric patients. In terms of



the pathogens identified by fecal PCR, patients infected with viruses primarily had BWT in the small intestine, while the terminal ileum and color were primarily affected in patients infected with bacteria. For most patients with BWT on abdominal CT, the symptoms improved spontaneously without progression to chronic intestinal disease. While adults with BWT require additional evaluations, we suggest simple observation and follow-up at OPD for pediatric patients.

The methods for measuring bowel wall thickness and the criteria for determining BWT on abdominal CT have been reported in various ways, but unified criteria have not been established, even in adults [8]. In some adult studies, the normal thickness of the small intestine in a dilated state was defined as 1–2 mm or less than 2–3 mm [9]. On the other hand, the normal colonic wall thickness was suggested to be within 3 mm in a dilated state. However, no studies have reported the diagnostic value of the bowel wall thickness or the criteria for determining BWT on abdominal CT among children, though a systematic review and meta-analysis of normal intestinal wall thickness in healthy children using ultrasonography was published recently [10]. Moreover, it is challenging to measure bowel wall thickness because it is a dynamic value related to bowel factors, such as folding, partial distension, or filling with fluids or feces [11]. In children, it is more difficult to identify BWT because the normal bowel wall thickness increases with age [12]. However, the MT/NT ratio could provide an objective measure by decreasing the error or interference caused by various bowel conditions, age, and individual differences. This study presented the MT/NT ratio as a novel method for measuring bowel wall thickness in children.

Several investigations have attempted to evaluate the clinical relevance of BWT findings on abdominal CT scans, but most were performed on adults [13]. Studies on adults have indicated that these findings require additional evaluation and endoscopy to rule out malignancy [4]. However, the clinical implications of BWT on abdominal CT cannot be the same for children who have a low risk of intestinal malignancy. This study showed that when BWT was detected on abdominal CT, 75.6% of the patients were diagnosed and treated based on the abdominal CT findings, fecal PCR results, and clinical symptoms. In comparison, the remaining 24.4% were designated into the non-gastroenteritis group and recovered spontaneously or did not progress to chronic intestinal disease. This was consistent with the results of a previous pediatric study showing that BWT on abdominal CT was a nonspecific finding in children [2]. In a recent pediatric retrospective study, colonic wall thickening on abdominal CT showed moderately strong agreement (κ =0.46) with endoscopic findings [14]. Therefore, in children, findings of BWT on abdominal CT might be appropriately addressed with clinical observation and follow-up and may not require prompt additional evaluation, unlike in adults.

The distribution of BWT differed according to the pathogens identified by fecal PCR. BWT was most often distributed in the small intestine in patients infected with viruses and in the terminal ileum and colon in patients infected with bacteria. Stool culture has been routinely used to identify pathogens, despite having low sensitivity and being time-consuming. Recently, approaches for the direct and rapid identification of multiple pathogens in stool specimens have been developed using PCR-based methods [15]. Using multiplex PCR for fecal samples rather than invasive endoscopy as an initial evaluation method is recommended to improve the diagnosis in children with BWT.

One of the strengths of our study was the relatively large number of pediatric patients with findings of BWT on abdominal CT. To our knowledge, there is only one pediatric study in the

recent literature addressing the clinical impact of BWT, but it involved a small population [2]. In addition, this study was meaningful because it was the first to suggest an objective method for measuring bowel wall thickness and the MT/NT ratio in each patient to negate the effect of interfering factors, such as bowel condition, interpersonal differences, and age. Further studies are needed to validate new pediatric criteria and apply them in practice.

As for this retrospective study's limitation, we could not confirm the patients' follow-up conditions based on objective radiological evaluations. Because most patients' symptoms improved spontaneously, we confirmed the undiagnosed patients' condition using medical chart reviews or telephone follow-up. Repeated CT scans in children are limited because of the risk of radiation exposure. Other limitations include selection bias since not all patients presenting with gastrointestinal symptoms at our hospital undergo abdominal CT because the decision to undergo abdominal CT is clinician-dependent. The distribution of the diagnosis and the clinical implications of BWT could vary according to the indications for abdominal CT and the level of each institution. Despite these limitations, we recommend that when BWT is described in an abdominal CT report of a pediatric patient in the absence of any other clinical explanation, it should be observed without further evaluation.

In conclusion, the present study presented a novel and objective method for measuring the bowel wall thickness as a ratio of the thicknesd to the normal bowel wall and provided a reference value for the thickness of the bowel wall in the small bowel and colon in children. This study found that BWT observed on abdominal CT in children might indicate nonspecific findings that can be observed and followed up without additional prompt evaluation, unlike in adults, because most of the patients' symptoms improved spontaneously. These findings could guide physicians' evaluation of patients with CT findings of BWT and their management of pediatric patients. Moreover, using multiplex PCR for fecal samples as an initial evaluation could be recommended to improve the diagnosis in undiagnosed children with BWT. To our knowledge, this was the first study to present a new method for measuring bowel wall thickness on abdominal CT in children and determine its clinical significance in a pediatric Asian population.

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