ORIGINAL ARTICLE

Factors Associated with False Negative Results of Contrast Enema for Diagnosis of Hirschsprung's Disease

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Background: The contrast enema diagnosing Hirschsprung's disease had a high false-negative rate, meaning that even if Hirschsprung's disease was suspected, the first contrast enema could not diagnose this disease.

Objective: To examine factors associated with the false-negative contrast enema.

Materials and Methods: Retrospective chart reviews of patients with Hirschsprung's disease underwent pull-through operations at Siriraj University Hospital between November 2006 and January 2021 were carried out.

Results: The sensitivity of the contrast enema was 82.6%. In the 190 patients with contrast enema, 30 out of 172 (17.4%) had false-negative results. To study the associated factors of false-negative contrast enema, the true-positive contrast enema, which was 142, was compared with a false-negative one, which was 30. The median age of the first contrast enema in the true-positive group was 26.6 days and false-negative group was 23.2 days, which was similar (p=0.581). The locations of the transitional zone in any segments of colon had no effect on false-negative contrast enema except for total colonic aganglionosis (TCA). Receiver operating characteristic (ROC) curves and areas under ROC were performed to assess the optimal cut-off value of the interval of rectal examination/rectal wash out withhold prior to contrast enema to predict false-negative. A higher false-negative rate in patients who discontinued the rectal examination of less than two days before the contrast enema than those with two days or more was found (p=0.125). The discontinued interval of rectal irrigation of less than one day before performing the contrast enema affected higher false-negative rates (p=0.091).

Conclusion: Age and locations of the transitional zone were not associated with false-negative contrast enema except for TCA. Too short, discontinued intervals of rectal examination, of less than two days and/or rectal irrigation of less than one day before contrast enema were associated with higher false-negative rates.

Keywords: Hirschsprung; Megacolon; Contrast enema; Barium enema; Diagnosis

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The diagnosis of Hirschsprung's disease can be done as the rectal suction biopsy is accepted as the gold standard diagnosing test for Hirschsprung's disease. No neurons are found in either the myenteric ganglion or the submucosal ganglion. Hypertrophic nerve fibers are also found. In addition, increased acetyl cholinesterase (Ache) activity is observed in either the submucosal layer or submucosal ganglion. In the previous studies, sensitivity of more than 90% and specificity of more than 95% were reported for rectal suction biopsy[1-4]. However, rectal suction biopsy in Thailand is limited due to the lack of a pathologic center to perform Ache activity detection.

Anorectal manometry is a test evaluating the recto-anal inhibitory reflex (RAIR). The absence of RAIR can diagnose Hirschsprung's disease with 75% to 100% sensitivity and 85% to 95% specificity[1,2,4,5]. However, anorectal manometry in Thailand is also limited due to the lack of a neonatal size of the probe and children's mobility during measurement.

Although the contrast enema is reported to have a sensitivity of 65% to 80% and a specificity of 65% to 100%[1,2], which is low compared to other tests, it is the most common test used in Thailand. Awareness of its accuracy is of high concern. Following contrast enema, a diagnosis of Hirschsprung's disease is characterized by the following:

A. The transitional zone is seen in Hirschsprung's disease[6]. The transitional zone arises from the

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difference in size of the bowels between the proximal dilated ganglionic bowel and the distal non-dilated aganglionic bowel.

B. Recto-sigmoid index (the ratio of rectal diameter/sigmoid diameter) of less than 1.0 is useful in the diagnosis of Hirschsprung's disease[7].

C. The presence of contrast retention in the proximal location of the sigmoid colon after 24 hours following a contrast enema may aid in the diagnosis[6].

D. The detection of irregular contractions of the aganglionic segment contributes to the diagnosis of Hirschsprung's disease[1,6].

The problem with the contrast enema is the high false negative rate[1,2], meaning that in patients with histologically confirmed Hirschsprung's disease, the contrast enema initially could not diagnose this disease, leading patients to undergo multiple contrast enema examinations. Factors contributing to the false negatives of a contrast enema include:

1. Age of the patient. If the patient is too young, the transitional zone may not be seen[1,6,8]. Because, at a young age, the proximal portion of the bowel with a ganglionic segment is not enlarged until the transitional zone is clearly visible.

2. The location of the transitional zone in Hirschsprung's disease is mostly located at or near the rectosigmoid junction. At that position, Hirschsprung's disease could be diagnosed by contrast enema[6]. But in cases where the transitional zone is located proximal to the distal descending colon, known as the long segment Hirschsprung's disease, contrast enema provides a less accurate diagnosis[9,10].

3. Rectal enema or rectal irrigation before contrast enema may be a factor contributing to a false negative contrast enema[11]. It is believed that rectal enema or rectal irrigation may shrink the proximal dilated ganglionic bowel compared to the distal non-dilated aganglionic segment. This may obscure the transitional zone.

4. Per rectal (PR) examination, it has been argued that PR before contrast enema may produce a false negative contrast enema[11].

In Thailand, the contrast enema is the most widely used diagnostic test for Hirschsprung's disease. The factors associated with the false-negative effect of the contrast enema test need to be clarified. Thus, the present study was conducted to find out how to decrease the interfering factors to reduce the false-negative contrast enema.

Materials and Methods

After obtaining approval from the Siriraj Institutional Review Board (COA. No Si 940/2020), a retrospective study was conducted in children with histologically confirmed Hirschsprung's disease operated on with a transanal endorectal pull-through (TERPT) or abdominal assisted TERPT or other pull-through operations in Siriraj University Hospital between November 2006 and January 2021, regardless of prior operations from other hospitals.

Patients with Hirschsprung's disease that previously undergone colostomy or ileostomy, unobtained and/or retrieved the radiologic finding of the contrast enema, patients who could not be diagnosed as Hirschsprung's disease by contrast enema and did not receive the definite operation for Hirschsprung's disease, Hirschsprung's disease patients associated with anorectal malformations, or patients with incomplete medical records, were excluded from the study.

In the present study, contrast enema included either barium or water-soluble contrast media. Barium contrast enema was sometimes performed by five experienced pediatric radiologists from the Department of Radiology, Faculty of Medicine, Siriraj University Hospital, whereas water-soluble contrast enema was conducted by either five experienced pediatric radiologists or six experienced pediatric surgeons at the Division of Pediatric Surgery, Department of Surgery, Faculty of Medicine, Siriraj University Hospital. All staff have had experience of performing the contrast enema for more than six years.

False negative of contrast enema means:

1. Patients received more than one contrast enema. At first, Hirschsprung's disease could not be diagnosed, but could be diagnosed by another contrast enema done later.

2. Hirschsprung's disease could not be firmly diagnosed by the first contrast enema, however, the operation for Hirschsprung's disease was performed, and the pathological results confirmed the diagnosis as Hirschsprung's disease.

Patients' demographic data, date of birth, the age of the first contrast enema, location of the radiologic and pathological transitional zone, duration of discontinued PR (days) prior to the contrast enema, and duration of discontinued rectal normal saline solution (NSS) irrigation (days) prior to the contrast enema, were collected. Single stage TERPT or abdominal assisted TERPT were preferred operations for Hirschsprung's disease. In some cases, Duhamel

operations were performed due to the surgeon's preference. The pathological reports were reviewed.

Data were collected and analyzed with IBM SPSS Statistics for Windows, version 27.0 (IBM Corp., Armonk, NY, USA). Quantitative data were expressed as median and range (min, max), and qualitative data were expressed as numbers and percentages. The Pearson chi-square test, Yates' continuity correction, or Fisher's exact test were used for investigating the associated factors of false negative results of contrast enema. A receiver operating characteristic (ROC) curve and area under ROC (AUC) were performed to assess the optimal cut-off value of the discontinued interval of PR prior to contrast enema (days) and the discontinued interval of rectal irrigation prior to contrast enema (days) to predict a false negative. An AUC of 0.5 suggested no ability to diagnose patients with or without false negative results, 0.7 to 0.8 was considered acceptable, 0.8 to 0.9 was considered excellent, and more than 0.9 was considered outstanding[12]. A p-value of less than 0.05 indicated statistical significance.

Results

Two hundred ninety-four patients underwent contrast enema. One hundred twenty-two patients were excluded because 78 patients lacked the results of the first contrast enema, 26 patients had never undergone definitive surgery, and 18 patients had the pathological reports that could not conclude the diagnosis of Hirschsprung's disease, but their contrast enema results were diagnosed as Hirschsprung's disease, thus, false positive results from the contrast enema. In the present study, there were 172 patients with histologically confirmed Hirschsprung's disease that met all inclusion criteria.

One hundred ninety patients underwent the first contrast enema. To study the false positive rate, false negative rate, sensitivity, positive likelihood ratio, positive predictive value, and accuracy of contrast enema to diagnose Hirschsprung's disease, all patients with the first contrast enema were studied. Because patients who could not be diagnosed as Hirschsprung's disease by contrast enema and did not receive a definite operation for Hirschsprung's disease were excluded due to lack of pathological reports, true negative results of contrast enema could not be declared in some cases. When true negative results could not be calculated, other parameters such as specificity, negative likelihood ratio, and negative predictive value, were also unable to be demonstrated. Among these 190 patients, false positives occurred in 18 of 190 (9.5%). There were 30 out of 172 (17.4%) that had false negative results. False negative results meant that Hirschsprung's disease was confirmed by pathological reports but could not be diagnosed as Hirschsprung's disease by the first contrast enema. False positive rate, false negative rate, sensitivity, positive likelihood ratio, positive predictive value, and accuracy of contrast enema diagnosing Hirschsprung's disease compared to pathological results are demonstrated in Table 1.

Table 1. False positive rate, false negative rate, sensitivity, positive likelihood ratio, positive predictive value, and accuracy of contrast enema diagnosis as Hirschsprung's disease compared to the pathological results were demonstrated

	n=190
True positive	142
False positive	18
False negative	30
Sensitivity (%)	82.6 (95% CI 73.2 to 87.5)
Positive likelihood ratio	0.826 (95% CI 0.842 to 1.005)
Positive predictive value (%)	88.7 (95% CI 82.9 to 92.8)
Accuracy (%)	74.7 (95% CI 68.1 to 80.4)

CI=confidence interval

One hundred seventy-two patients were confirmed as Hirschsprung's disease by the pathological report, 127 patients were male, and 45 patients were female. The median age of the first contrast enema was 26.1 days of age. Contrast enemas were performed with 62.1% barium enema and 37.9% other water-soluble contrast enemas. Of the 172 patients, 111 underwent TERPT and 61 underwent abdominal-assisted TERPT. The patients who underwent the Duhamel operation had false positive contrast enema, therefore, they were not included in the present study due to unconfirmed Hirschsprung's disease. The locations of the transitional zone were mostly located at the rectum in 15.1% and rectosigmoid colon in 45.9%. Sigmoid colon was the transitional zone in 14.5% and the long segment Hirschsprung's disease proximal to sigmoid colon was 24.4%.

A comparison between the group with true positive contrast enema, which was 142, and the group with false negative contrast enema, which was 30, was performed to study the associated factors affecting the false negative contrast enema. The factors that might be associated with the false results of contrast enema, composed of the age of the first contrast enema, the location of the transitional zone, types of operation, the discontinued interval of PR, and the discontinued interval of rectal NSS irrigation prior to the contrast enema, were studied.

Table 2. Patients with Hirschsprung disease's data, such as age of the first contrast enema, types of surgery, locations of transitional zone (T-zone), discontinued interval of PR prior to contrast enema, and discontinued interval of rectal NSS irrigation prior to contrast enema: comparison between true positive and false negative contrast enema

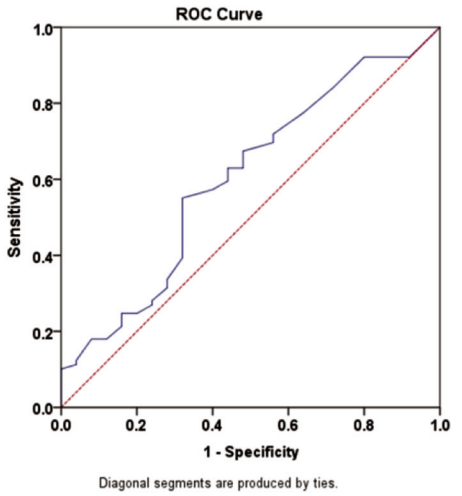
Variable	Total (n=172)	Positive contrast enema (n=142)	Negative contrast enema (n=30)	p-value
Sex; n (%)				0.035
Male	127 (73.8)	111 (78.1)	16 (53.3)	
Female	45 (26.2)	31 (21.8)	14 (46.6)	
Age of the first contrast enema (days)				0.581
Median (min, max)	26.1 (1, 5,288)	26.6 (1, 5,288)	23.2 (1, 1,474)	
Type of the surgery; n (%)				0.953
TERPT	111 (64.5)	91 (64.0)	20 (66.6)	
Abdominal assisted TERPT	61 (35.4)	51 (36.0)	10 (33.3)	
Location of the T-zone; n (%)				
Rectum	26 (15.1)	22 (15.5)	4 (13.3)	0.538
Rectosigmoid colon	79 (45.9)	65 (45.8)	14 (46.7)	1.000
Sigmoid colon	25 (14.5)	19 (13.4)	6 (20.0)	0.125
Descending colon	15 (8.7)	14 (9.9)	1 (3.3)	0.697
Splenic flexure	9 (5.2)	9 (6.3)	0 (0)	0.364
Transverse colon	4 (2.3)	3 (2.1)	1 (3.3)	1.000
Ascending colon	7 (4.1)	6 (4.2)	1 (3.3)	1.000
Ileum	7 (4.1)	4 (2.8)	3 (10.0)	0.058
Discontinued interval of PR prior to contrast enema (days)	(n=114)	(n=89)	(n=25)	
Median (min, max)	3.0 (0, 27.6)	3.0 (0, 27.6)	2.0 (0, 10.8)	0.188
Discontinued interval of rectal NSS irrigation prior to contrast enema (days)	(n=95)	(n=74)	(n=21)	
Median (min, max)	1.0 (0, 10)	2.0 (0, 10)	1.0 (0, 4)	0.170

TERPT=transanal endorectal pull-through; PR=per rectal; NSS=normal saline solution

All information is demonstrated in Table 2.

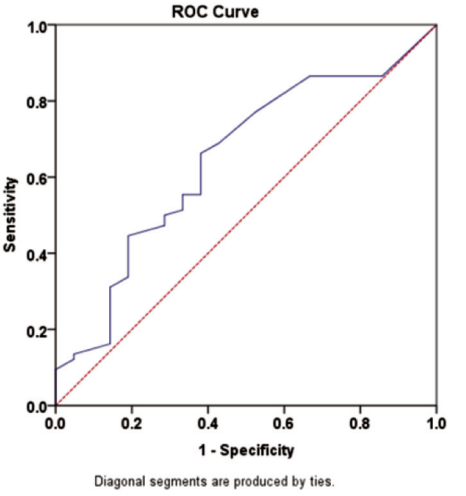
The median age of the first contrast enema in the true positive group and the false negative group was 26.6 and 23.2 days, respectively. This difference was not statistically significant (p=0.581). The p-value comparing the difference between these two groups in the short segment Hirschsprung's diseases revealed no statistical significance at any location. The p-values comparing the differences between positive contrast enema and false negative contrast enema of the rectum, rectosigmoid, and sigmoid colon were p=0.538, p=1.000, p=0.125, respectively. The p-value comparing the differences between positive contrast enema and false negative contrast enema in long segment Hirschsprung's diseases revealed no statistical significance at any locations except the transitional zone located at the ileum for total colonic aganglionosis or TCA, in which the difference was nearly a statistically significant difference (p=0.058). The p-values comparing the differences between true positive contrast enema and false negative contrast enema of the descending colon, splenic flexure, transverse colon, and ascending colon were p=0.697, 0.364, 1.000, and 1.000, respectively.

According to Table 2, the median of the discontinued interval of PR prior to contrast enema in the false negative group was 2.0 days, whereas the median of this interval in the true positive group was 3.0 days. A ROC curve and AUC to assess the optimal cut-off value of the discontinued interval of PR prior to contrast enema to predict the false negative of contrast enema are demonstrated in Figure 1. The AUC of the discontinued interval of PR prior to contrast enema was 0.603 (95% CI 0.455 to 0.751). This data showed an ability to discriminate between patients with true positive and false negative contrast enemas[12]. Therefore, the practical cut-off value from the coordinates of the curves was two days of the discontinued interval of PR prior to contrast enema (p=0.11). Two days of the discontinued interval of PR prior to the contrast enema were used as the intersection to find the correlation (Table 3). The results showed a higher false-negative rate in patients who underwent PR less than two days before the contrast enema compared with those underwent PR more than or equal to two days before the contrast enema was 60% versus 40% (p=0.125) (Table 3).



AUC=0.603 (95% CI 0.455 to 0.751)

Figure 1. ROC curve and AUC of the discontinued interval of PR prior to contrast enema to predict the false negative of contrast enema.



AUC=0.645 (95% CI 0.512 to 0.779)

Figure 2. ROC curve and AUC of the discontinued interval of rectal NSS irrigation prior to contrast enema to predict the false negative of contrast enema.

Table 3. The discontinued interval of PR prior to contrast enema cross tabulation with the false negative results

	False negative; n (%)		p-value
	Yes (n=20)	No (n=94)	
The discontinued interval of PR before contrast enema			0.125
<2 days	12 (60.0)	36 (38.3)	
≥2 days	8 (40.0)	58 (61.7)	

PR=per rectal

Table 4. The discontinued interval of rectal NSS irrigation prior to contrast enema cross tabulation with the false negative results

	False negative		p-value
	Yes (n=16)	No (n=79)	
The discontinued interval of rectal NSS irrigation before contrast enema			0.091
<1 day	12 (75.0)	38 (48.1)	
≥1 day	4 (25.0)	41 (51.8)	

NSS=normal saline solution

According to Table 2, the median of the discontinued interval of rectal NSS irrigation prior to contrast enema in the false negative group was 1.0 days, whereas the median of the true positive group was 2.0 days. A ROC curve and AUC to assess the optimal cut-off value of the discontinued interval of rectal NSS irrigation prior to contrast enema to predict the false negative of contrast enema are demonstrated in Figure 2. The AUC of the discontinued interval of rectal NSS irrigation prior to contrast enema was 0.645 (95% CI 0.512 to 0.779). Similar to the discontinued interval of PR prior to contrast enema, these data also demonstrated ability to discriminate between patients with true positive and false negative contrast enema[12]. Therefore, the practical cut-off value from the coordinates of the curves was one day of the discontinued interval of rectal NSS irrigation prior to contrast enema (p=0.043). One day of the discontinued interval of rectal NSS irrigation prior to contrast enema was used as the intersection to find the correlation (Table 4). Along with rectal NSS irrigation, discontinuation less than one day before performing the contrast enema affected higher of the false-negative rates compared with those who discontinued more than or equal to one day before the contrast enema at 75.0% versus 25.0% (p=0.091) (Table 4).

Discussion

There are three confirmation methods for the diagnosis of Hirschsprung's disease, rectal suction biopsy, anorectal manometry, and contrast enema. Rectal suction biopsy is accepted as the gold standard for diagnosing Hirschsprung's disease with a sensitivity greater than 90% and a specificity greater than 95%[1-4]. In Thailand, this has a very limited role due to a lack of a pathological center to perform laboratory detecting Ache activity. Anorectal manometry, which is reported with 75% to 100% of sensitivity and 85% to 95% of specificity[1,2,4,5] also has limitation in Thailand due to lack of appropriate balloon size for neonates.

Because there was no other accurate investigation, the contrast enema is the most commonly used diagnostic method in Thailand. The gastrointestinal contrast study not only diagnosed Hirschsprung's disease but could diagnose other gastrointestinal motility disorders in children[13]. Contrast enema is reported to have a sensitivity of about 65% to 80% and a specificity of 65% to 100%[1,2], which is low compared to other tests. Awareness of its accuracy is concerning.

Using contrast enema examination, a diagnosis of Hirschsprung's disease is characterized by the following:

A. The transitional zone is seen in Hirschsprung's disease. The transitional zone arises from the difference in size between the proximal dilated ganglionic bowel and the distal non-dilated aganglionic bowel. The transitional zone is the most common at 83.33% of imaging finding of contrast enema for Hirschsprung's disease[14]. The transitional zone of Hirschsprung's disease is mostly at or near the rectosigmoid junction. If the transitional zone could be seen, a diagnosis could be made[6,15].

B. The recto-sigmoid index was calculated using the method described by Pochaczevsky and Leonidas[7]. Measurements were made in antero-posterior and lateral projection and obtained along a transverse axis, vertical to the longitudinal axis of the colon at that point. Recto-sigmoid index was the widest diameter of the rectum/the widest diameter of the sigmoid. Normally, the rectum is larger than the sigmoid colon, so the recto-sigmoid index is greater than one. In Hirschsprung's disease, the transitional zone is usually at or near the rectosigmoid junction. In those cases, the size of the rectum is smaller than the sigmoid colon. A recto-sigmoid index less than one is useful in diagnosis[7]. The reverse recto-sigmoid ratio was found in 35.41% of contrast enema diagnosed Hirschsprung's disease[14].

C. The presence of contrast retention in the proximal location of the sigmoid colon after 24 hours after a contrast enema may aid in the diagnosis[4,6,16]. A study by Gupta and Guglani concluded that prolonged retention of barium in the sigmoid colon not only aided in diagnosis but was a strong indicator of Hirschsprung's disease[17]. However, this finding is not specific. Fourteen percent of patients with Hirschsprung's disease had no contrast retention in the proximal intestine to sigmoid colon after 24 hours following contrast enema[6].

D. The irregular contractions of the aganglionic segment contribute to the diagnosis of Hirschsprung's disease[1,6]. The colonic wall irregularity of the aganglionic segment was named "sawtooth appearance" and found in 18.75% of contrast enema for Hirschsprung's disease[14].

In the present study, the sensitivity of the contrast enema was 82.6%. The problem with contrast enema is its high false negative rate. In the present study 190 contrast enema, false positives occurred in 18 out of 190 (9.5%). There were 30 out of 172 (17.4%) false negative results. False negative results meant patients with Hirschsprung's diseases, confirmed by pathological reports, could not be diagnosed with Hirschsprung's disease by the first contrast study. False negatives have led patients to undergo multiple contrast enema examinations. Initially, the proximal ganglion-containing part of the colon was less dilated, but as time passed, the proximal ganglionic intestine was more enlarged. When doing a re-contrast enema, the transitional zone is clearly visible due to the difference in size of the distal non-ganglion rectum, which is much smaller than the proximal ganglionic segment. The study of the factors associated with the false-negative contrast enema will be of great benefit. All reported important associated factors, which age at the first contrast enema, location of the transitional zone, PR, and rectal irrigation prior to the contrast enema, were studied.

The age of the patient at the time of the first contrast enema was studied. Previous studies reported that if the patient was too young, the transitional zone may not be seen[1,6,8,14,18]. At a younger age, the proximal ganglionic segment of the bowel is not enlarged, therefore, the transitional zone might not be clearly visible. A study reported that in only 75% of patients with less than one month of age, the transitional zone could be seen[10]. In the present study, the median age of the first contrast enema in the true positive group and the false negative group was 26.6 and 23.2 days, respectively. This difference was not statistically significant (p=0.581). This information did not suggest that younger child had a higher false negative rate of contrast enema as previous publications[1,6,8,18]. This might be explained by the fact that in other developed countries, rectal suction biopsy is much more preferred than contrast enema, and the pediatric surgeons there tend to do rectal suction biopsy before any contrast enema. Despite debates regarding the accuracy of contrast enema in the newborn period, contrast enema is still the mainstay of the diagnostic method for Hirschsprung's disease in Thailand. It also provides an estimation of the proximal extent of aganglionosis

bowel as well[19].

The location of the transitional zone of Hirschsprung's disease is mostly at or near the rectosigmoid junction. In that location, the transitional zones are often clearly seen with a contrast enema, and a diagnosis of Hirschsprung's disease could be made[6]. In cases where the transitional zone is proximal to the distal descending colon, known as long segment Hirschsprung's disease, contrast enema provides a less accurate diagnosis[9,10,14,18,20]. In the present study, the differences between true positive contrast enema and false negative contrast enema rates in each location of the transitional zone in short segment Hirschsprung's diseases revealed no statistical significance at any locations. The differences between true positive contrast enema and false negative contrast enema rates in each location of the transitional zone in long segment Hirschsprung's diseases revealed no statistical significance in any locations except the transitional zone located at the ileum in which the difference is nearly statistically significant. In TCA, the transitional zone located at the ileum, it still had a high false negative rate of contrast enema (p=0.058).

The size of the aganglionic colon in the long segment Hirschsprung's disease varies greatly[18], therefore, contrast enema has limited diagnostic efficiency in patients with TCA[9,18]. Even with the assumption that the size of the colon in TCA is smaller than that in usual Hirschsprung's disease, one reported that in up to 75% of patients with TCA, normal colon size could be found[21].

PR has been argued that PR before contrast enema may produce false negatives of contrast enema[11], but a study had argued against that[6]. Rectal enema or rectal irrigation before contrast enema may be a factor contributing to a false negative contrast enema[11]. It was believed that rectal enema or rectal irrigation may shrink the dilated ganglionic bowel proximal to the non-dilated aganglionic segment. This may obscure the transitional zone. Studies reported that rectal enema prior to contrast enema did not produce false negative results[6,10].

At the Division of Pediatric Surgery, Department of Surgery, Faculty of Medicine Siriraj University Hospital, PR and rectal enema or rectal irrigation are usually refrained approximately three days prior to the contrast enema, in the belief that the PR or repeated enema may obscure the transitional zone and the precise transitional zone would not be achieved[19]. Following the contrast enema, further bowel preparation with rectal NSS irrigation in the average amount of 30.3±1.0 mL/kg/dose per session twice a day was done[22].

Whether PR and rectal enema or rectal NSS irrigation before contrast enema may be the factors contributing to false negative contrast enema, ROC curves and AUC were performed to assess the optimal cut-off values of the discontinued interval of PR prior to contrast enema and the discontinued interval of rectal NSS irrigation prior to contrast enema to predict a false negative. The AUC of the discontinued interval of PR prior to contrast enema was 0.603 and the AUC of the discontinued interval of rectal NSS irrigation was 0.645. Both of them showed an ability to discriminate between the patients with true positive and false negative contrast enema[12] (Figure 1, 2).

From the present study data, the practical cut-off value from the coordinates of the curves was two days of the discontinued interval of PR prior to contrast enema (p=0.11) and one day of the discontinued interval of rectal NSS irrigation (p=0.043). Therefore, two days of discontinued interval of PR and one day of discontinued rectal NSS irrigation before performing contrast enema were decided as the intersection to find the correlation (Table 3, 4). The results showed a higher false-negative rate in patients who underwent a discontinued interval of PR less than two days before the contrast enema compared with those discontinued more than or equal to two days before the contrast enema at 60% versus 40% (p=0.125) (Table 3). Along with the discontinued interval of rectal NSS irrigation, discontinuation less than one day before performing the contrast enema affected higher false-negative rates compared with those more than or equal to one day prior to the contrast enema at 75.0% versus 25.0% (p=0.091) (Table 4). From the present study data, it implies that the too-short, discontinued interval of PR of less than two days and discontinued interval of rectal NSS irrigation of less than one day prior to contrast enema were associated with more false-negative rates of contrast enema.

In addition to the accuracy of the contrast enema in diagnosing Hirschsprung's disease, the discrepancy in the position of transitional zones between the radiologic transitional zone and the pathologic transitional zone should be considered. The locations of the radiologic transitional zone corresponded with the pathological location in 89% to 91% of the short segment Hirschsprung's disease[9,19]. However, in patients with the long segment Hirschsprung's disease or TCA, the correspondence between the location of the pathologic and radiologic transitional zones

was only 31%[9]. A frozen section of the distal pull-through colon before coloanal anastomosis should be emphasized. In the authors' previous publication, retained aganglionosis was still found in 3% of abdominal assisted pull-through operations, even if laparotomy was done[22].

Limitation

First, the present study was designed retrospectively, which means that there may be missing information. Of the total reviewed 294 patients with Hirschsprung's disease, the total included population of the present study was 172. Of the excluded 122 patients, a lack of results from the first contrast enema was noted in 78 patients. Moreover, the accuracy of the radiologic diagnosis for Hirschsprung's disease would vary depending on the individual staff who interpreted the results.

Second, the number of patients with false negative contrast enemas was small. There were 30 out of 172 (17.4%) false negative contrast enemas, which is a small number compared to other studies. This made it challenging to find significant risk factors in these 30 patients who had false negative contrast enemas. Further research is needed for a larger population.

Third, the generalizability of the present study findings is limited. The study was conducted in a single university hospital, and as such, the method and technique used by the radiologist and pediatric surgeons to perform and interpret the contrast enema may differ from those used in other institutions.

Conclusion

The sensitivity of the contrast enema was 82.6%. In the 190 patients with contrast enema, 18 out of 190 (9.5%) were false positives and 30 out of 172 (17.4%) were false negatives. The median age of the first contrast enema in the true positive group was 26.6 days and false negative group was 23.2 days, which was similar (p=0.581). The locations of the transitional zone in any segments of the colon had no effect on false negative contrast enema except for TCA. Too-short, discontinued intervals of PR of less than two days and rectal irrigation of less than one day prior to contrast enema were associated with higher false-negative rates. However, the number of patients with false negative contrast enema was small. Further research is needed on a larger population.

What is already known on this topic?

The contrast enema diagnosing Hirschsprung's disease had a high false-negative rate, meaning that even if Hirschsprung's disease was suspected, the contrast enema could not first diagnose this disease.

What does this study add?

Age and location of transitional zone were not associated with false-negative contrast enema except for TCA. Too-short, discontinued intervals of PR of less than two days and rectal irrigation of less than one day prior to contrast enema were associated with higher false-negative rates.

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Conflicts of interest

The authors declare no conflicts of interest.

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