

Validation and modification of the 'Chiang Mai University Intussusception scoring system' used to predict failure of non-surgical treatment in infantile intussusception

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ABSTRACT

Background This study aimed to validate and modify the recently released Chiang Mai University Intussusception (CMUI) scoring system in predicting failure of non-surgical management of infantile intussusception.

Methods A retrospective review was conducted in 151 cases of infantile intussusception who were primarily treated with pneumatic reduction in our institute during 2008–2018. The analysis focused on the validation of the CMUI scoring system. Following this analysis, the scoring system was modified to be more suitable for our clinical practice, in which we perform pneumatic reduction in all cases.

Results Pneumatic reduction was successfully performed in 120/151 cases (79.5%). A high CMUI score was significantly associated with increased likelihood of failure at the positive likelihood ratio of 1.49 (sensitivity 25.8 and specificity 82.7). The area under the receiver operating characteristic curve (AUC) was 0.73. We modified the CMUI System in two ways, first by removing the item 'method of reduction' and replacing it with 'hyponatremia', and by changing the definition of low body weight to less than 9 kg. The modified CMUI had an AUC of 0.76. A high score (>9 points) on the modified version gave a positive likelihood ratio of 4.77 (sensitivity 53.0 and specificity 80.9).

Conclusion In infantile intussusception primarily treated with pneumatic reduction, the modified CMUI scoring system gave a better prediction reliability than the original.

INTRODUCTION

Intussusception is the most common cause of acute abdominal emergency that requires surgical treatment in infants under 2 years of age.^{1 2} The global incidence of infantile intussusception is around 1–4:1000 live births with no particular ethnic preponderance.^{1 3} In Thailand, a study from a large pediatric surgical center in Bangkok reported an annual average of 60 new cases during the years 1999–2008.⁴ In our institute, which is the largest teaching hospital in southern

Key messages

What is already known about this subject?

- ▶ Intussusception is one of the most common surgical emergencies in infants.
- ▶ First-line treatment of intussusception is pressure reduction known as non-surgical management. Those who failed non-surgical management require surgery.
- ▶ Various scoring systems have been constructed with an aim to predict chance of an intussusception to be reduced by non-surgical mean, including the recent Chiang Mai University Intussusception (CMUI) scoring system.

What are the new findings?

- ▶ Validation of the original CMUI scoring system using an independent data set proved that the scoring system can be used with acceptable specificity (82.7%) but low sensitivity (25.8%).
- ▶ Strong predictors for failure of non-surgical management include rectal bleeding and unfavorable ultrasound signs.
- ▶ Some modifications of the score may result in better sensitivity.

How might it impact on clinical practice in the foreseeable future?

- ▶ In view of patient safety, the results of non-surgical treatment in infantile intussusception should be predicted and prompt surgical referral should be prepared in a case with high chance of failure. CMUI scoring system or its modification can be used as a prediction tool in the treatment algorithm.

Thailand, previous studies have shown an increasing incidence from an approximate number of 5 cases per year during the years 1983–1997⁵ to 10 cases per year in the period 2002–2007.⁶

Management of intussusception usually begins with resuscitation and when there are no contraindications, the patient is



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prepared for a non-surgical reduction either by liquid or air enema.¹ Various studies have reported that, with air reduction, laparotomy could be avoided in 70%–90% of infantile intussusception cases.^{4 7 8} However, the remaining 10%–30% of the reported cases had failure of therapeutic enema, and required prompt surgical consultation and more intensive interventions. The ability to predict with some reliability cases which are more likely to fail non-surgical management would be of great benefit in allowing earlier surgical preparation. In addition, bypassing any attempt at non-surgical management in cases with a poor probability of successful reduction could also avoid complications caused by prolonged strangulation.⁹ Various clinical and radiologic factors have been reported as being associated with failure of non-surgical management for intussusception, which can be subcategorized into four groups: demographic factors, clinical symptoms, physical examination factors and imaging factors.^{6 10} Regarding demographic factors and clinical symptoms, younger age, longer duration of abdominal pain, rectal bleeding, presence of diarrhea, abdominal distension, and dehydration or vomiting are the main unfavorable factors. Physical signs of fever, palpable mass, left-side mass and weight loss are linked to failed enema reduction. Radiological signs of small intestinal obstruction, ascites, trapped fluid in the intussusception, thickened colonic wall and decreased blood flow into the incarcerated bowel have also been mentioned as predictors of failure.

Associations between these factors and clinical outcomes have varied among the reported series, which could be explained by variations in the treatment algorithms. In Thailand, previous studies from our team and another study from Chiang Mai University (CMU) both found that low weight (<12 kg), prolonged symptoms, rectal bleeding, high body temperature, advanced invagination to the left side and unfavorable ultrasound findings were associated with failure of non-surgical reduction. Recently, researchers in CMU have constructed a scoring system for prediction of reduction failure called the 'CMUI scoring system.'¹¹ Their study demonstrated that a patient with intussusception with a high score (>11) had a significant likelihood of failed reduction. The objective of the current study was to validate the Chiang Mai University Intussusception (CMUI) scoring system with an independent external set of infantile intussusception data. Following the validation of the original scoring system, small adjustments of the criteria to better reflect the infants treated primarily with pneumatic reduction were made.

METHODS

Patients and non-surgical management

The study was a retrospective cohort study which included consecutive cases of intussusception aged less than 5 years who were treated in Songklanagarind Hospital, the major tertiary-level medical center in southern Thailand,

during the period January 2008 to January 2018. Case identification used the Tenth Edition of the International Classification of Diseases and Related Health Problems version 10 code K56.1. All clinical and laboratory data were retrieved from the hospital electronic medical records under the approval of the Human Research Ethics Committee of the institute. Cases with contraindications for non-surgical reduction for whom a primary laparotomy was performed were excluded.

In our institute during the study period, non-surgical management of intussusception used pneumatic reduction performed under real-time X-rays (fluoroscopy) or ultrasonography. When intussusception was suspected, diagnostic confirmation was obtained by abdominal ultrasonography plus a plain radiograph. If there was no peritonitis nor unstable hemodynamics, the patient would be prepared for a pneumatic reduction with a readily surgical back-up alerted and ready if needed. Blood tests included a complete blood count and serum chemistry. A peripheral vein was accessed for fluid and drug administration. The procedure was performed under the pediatric sedation protocol of our institute which during the study period usually used light doses of fentanyl and midazolam. The details of the pneumatic reduction have been provided in our previous publications.⁶ For the procedure, briefly, air was insufflated via a plain rectal catheter connected with a sphygmomanometer. The applied pressure was usually between 80 and 120 mm Hg for a period not exceeding 3 min per trial. Failure of the non-surgical reduction was deemed when the intussusceptum could not be reduced into the terminal ileum after three to five trials or when pneumoperitoneum occurred. After a successful reduction, the patient was usually admitted overnight for parenteral support and monitoring. In cases of failed pneumatic reduction, an emergency laparotomy was performed. If indicated the decision for intestinal resection was made by the attending pediatric surgeon. All available radiographic images were accessed and reviewed on the Picture Archiving and Communication System (Fujifilm Medical System, Tokyo, Japan) of the hospital. Unfavorable ultrasound findings were deemed based on criteria derived from our previous study, which included colonic wall thickening, trapped fluid between bowel loops, ascites, signs of small bowel obstruction and absence of color flow.⁶ Electrolyte imbalances such as hyponatremia were identified based on hospital laboratory values.

The original CMUI prediction scoring system and our modifications

The CMUI scoring system was created by Khorana *et al* from CMU, Thailand,¹⁰ with an aim to be used as a predictor of failure in non-surgical treatment of intussusception. The scoring system consists of 10 items, that is, body weight less than 12 kg, duration of symptoms more than 48 hours, vomiting, rectal bleeding, abdominal distension, temperature more than 37.8°C, palpable mass, location, poor ultrasound signs, and method of

reduction. A score of 2 is assigned for each parameter except for the duration, the mass, the ultrasound signs and method of reduction which received 1 point if positive. A patient is defined as high risk if the total score is 12 or greater of 16 possible points.

The data set used to formulate the CMUI scoring system consisted of two sources, a set from one institution each in Bangkok and Chiang Mai, Thailand. The former used a hydrostatic barium enema as their preferential method of reduction when the latter used pneumatic reduction. In order to modify the scoring system to suit the clinical context of our institute where pneumatic reduction while the only choice of non-surgical management in reducing an intussusception during the study period, the study repeated the association analysis for each of the scoring parameters of the CMUI scoring system using our data set. In an attempt to replace the method of reduction with one or more other parameters, we performed an association study using parameters selected from our previous study by Kritsaneepaiboon *et al.*⁶ The modified score was then revalidated with the same data set.

Statistical analysis

Unless stated otherwise, all numerical data are presented as mean and SD or median with IQR as appropriate. Categorical data are presented in percentages. The association study used univariate logistic regression analysis. Comparisons of numerical data used Student's t-test or Wilcoxon rank-sum test according to the normality of their distribution. Univariate analysis used logistic regression and the results are presented as OR and 95% CIs. To help visualize correlations between the scores and the outcomes, a receiver operating characteristic (ROC) curve was created. Sensitivity and specificity analyses of the scoring systems used the cut-off value suggested by the original CMUI scoring system. All analyses were done with the Stata program V.13.0 (Texas, USA).

RESULTS

Demographic data

During the study period, a total of 158 cases of intussusception were treated in our institute. Among these, primary pneumatic reduction was performed in 151 cases (95.6%). The median age of the patients was 10 months (IQR 6, 20 months) and the median weight was 8.6 kg (IQR 7.8–11 kg). The median age in the failure group (7 months; IQR 5.5, 10.0 months) was significantly lower than in the successful reduction group (13.5 months; IQR 7, 21 months) ($p < 0.01$) and the median weight in the failure group (8 kg; IQR 6.9, 9 kg) was significantly lower than in the successful group (9 kg; IQR 7.9, 11.0 kg) ($p = 0.01$).

The success rate of pneumatic reduction during the study period was at 79.5% (120 of 151 cases). One case suffered inadvertent bowel perforation during the procedure. Among the 31 cases who were considered failed and manual reduction was performed, a portion of intestine

was resected because of necrosis in 6 (19.4%) cases. A pathologic lead point was found in one case, a 13-month male infant with a Meckel's diverticulum at the terminal ileum.

Validation of the original CMUI scoring system using our data set

When our data set was analyzed using the original CMUI scoring system, it was found that the total scores ranged from 0 to 15, with an average score of 8.0 points. Of our 151 cases, 19 patients (12.6%) had a high CMUI score (score 12–15 points). The average score in the failure group (9.3 points; SD 3.6 points) was significantly higher than that of the success group (7.4 points; SD 2.7 points, $p < 0.01$). Using a cut-off of 11 to indicate a high CMUI score, the positive likelihood ratio was 1.49 and the sensitivity and specificity were 25.8% and 82.7%, respectively (accuracy 78.1%). On ROC analysis, the area under the ROC curve of the CMUI scoring system was 0.73 and the cut-off with the highest sensitivity and specificity was 9 points (sensitivity 61.3%, specificity 82.5%, accuracy 78.1%).

On analysis of individual components in the CMUI scoring system with failure of non-surgical treatment, 4 in 10 items in the CMUI score, rectal bleeding, abdominal distension, location of the intussusceptum and unfavorable ultrasound signs, were significantly associated with the outcome (table 1). Among the ultrasound findings, presence of ascites and trapped fluid between bowel walls had the highest OR to predict failure of non-surgical management. On multivariate analysis, rectal bleeding, abdominal distension and unfavorable ultrasound signs were positively associated with failure of non-surgical reduction (table 2). Interestingly, multivariate analysis showed that low body weight (< 12 kg) was a protective factor for failed non-surgical management in our intussusception cases.

As the association between low body weight and failure was contradictory to our hypothesis, we tried to reanalyze this parameter using a cut-off weight of 9 kg. The univariate analysis found that weight ≤ 9 kg was significantly associated with higher chance of failed pneumatic reduction (28.2%, compared with 10.61% in those cases with body weight > 9 kg, OR 3.31, 95% CI 1.32 to 8.27). We further subcategorized body weight into three strata, 0–9 kg (85 cases), 9.01–13 kg (49 cases) and more than 13 kg (17 cases), and the analysis found that the incidences of failed pneumatic reduction in the three weight categories were 28.4%, 6.1% and 23.5%, respectively.

Modification of the CMUI scoring system

In order to identify parameters to replace the method of reduction, further association analysis was performed for factors selected from our previous study (table 3). We additionally found that a decrease of hematocrit to less than 30% and changes in serum electrolytes, including hyponatremia and hypokalemia, were significantly associated with failed non-surgical treatment. When all these

Table 1 Analysis of individual items in the CMUI scoring system and outcomes of non-surgical treatment

Parameters	All cases (n: 151)	Success group (n: 120)	Failure group (n: 31)	P value
Body weight (kg)				0.60
<12	124 (82.1%)	97 (78.2%)	27 (21.8%)	
≥12	27 (17.9%)	23 (85.2%)	4 (14.8%)	
Duration of symptoms (hours)				0.95
<48	103 (68.2%)	82 (79.6%)	21 (20.4%)	
≥48	48 (31.8%)	38 (79.2%)	10 (20.8%)	
Vomiting				0.10
Absent	42 (27.8%)	37 (88.1%)	5 (11.9%)	
Present	109 (72.2%)	83 (76.15%)	26 (23.9%)	
Rectal bleeding				<0.01
Absent	73 (48.3%)	67 (91.8%)	6 (8.2%)	
Present	78 (51.7%)	53 (67.9%)	25 (32.1%)	
Abdominal distension				<0.01
Absent	67 (44.4%)	61 (91.0%)	6 (9.0%)	
Present	84 (55.6%)	59 (70.2%)	25 (29.8%)	
Fever				0.42
Absent	120 (79.5%)	97 (80.8%)	23 (19.2%)	
Present	31 (20.5%)	23 (74.2%)	8 (25.8%)	
Palpable mass				0.10
Absent	97 (64.2%)	81 (83.5%)	39 (72.2%)	
Present	54 (35.8%)	39 (72.2%)	15 (27.8%)	
Location of intussusceptum				<0.01
Right	136 (90.1%)	114 (83.8%)	22 (16.2%)	
Left	15 (9.9%)	6 (40.0%)	9 (60.0%)	
Unfavorable ultrasound signs				<0.01
Absent	108 (71.5%)	98 (90.7%)	10 (9.3%)	
Present	43 (28.5%)	22 (51.2%)	21 (48.8%)	
Method of reduction				NA
Pneumatic reduction	151 (100%)	120 (79.5%)	31 (20.5%)	
Hydrostatic reduction	–	–	–	

CMUI, Chiang Mai University Intussusception; NA, not analyzed (the only non-surgical treatment in our institute is pneumatic reduction).

parameters were included in the logistic regression model, the three items were not independently associated with failed pneumatic reduction. Among those three, hyponatremia had the highest OR. Thus, finally, taking these things together, we considered two modifications: using weight cut-off of 9 kg instead of 12 kg and adding hyponatremia as a new scoring item. In addition, as unfavorable ultrasound findings had a stronger association with failed pneumatic reduction in both univariate and multivariate analyses, we considered to score this item 2 points and reduce the score of body weight <9 to 1 point, thus maintaining the highest possible score at 16 points. Table 4 summarizes our modified CMUI scoring system.

On ROC analysis, the modified CMUI scoring system had an area under the curve of 0.76 and the cut-off value

with the highest sensitivity and specificity was at 9 points. By using the cut-off point at 9, the modified scoring system had sensitivity and specificity to predict failure of non-surgical reduction of 53.0% and 88.9%, respectively, with a positive likelihood ratio of 4.77 and an accuracy of 80.6%. Comparing the original CMUI scoring system and the modified one at the same cut-off point of 9, the OR of high scores in the prediction of failure increased from 7.46 (95% CI 3.15 to 17.68) to 9.14 (95% CI 3.52 to 23.70) (figure 1).

DISCUSSION

Various clinical scoring systems have been implemented for use in assisting clinical decision-making such as Alvarado score in diagnosing acute appendicitis¹² and

Table 2 Univariate and multivariate logistic regressions of parameters predicting failed non-surgical management of intussusception

Parameters	OR (95% CI)	Adjusted OR (95% CI)	
		9 items from original CMUI	9 items+3 new candidates
Low body weight (<12 kg)	0.69 (0.26 to 1.81)	0.16 (0.37 to 0.77)	0.08 (0.01 to 0.55)
Prolonged duration of symptoms (>48 hours)	0.99 (0.43 to 2.30)	0.70 (0.23 to 2.07)	0.38 (0.11 to 1.33)
Vomiting	1.41 (0.56 to 3.58)	1.73 (0.50 to 5.98)	1.39 (0.35 to 5.64)
Rectal bleeding	5.26 (2.01 to 13.77)	3.61 (1.11 to 11.79)	6.14 (1.38 to 27.42)
Abdominal distension	4.31 (1.65 to 11.25)	3.36 (1.09 to 10.36)	2.66 (0.77 to 9.24)
Fever (body temperature >37.8°C)	2.75 (1.14 to 6.62)	1.68 (0.56 to 5.08)	1.70 (0.50 to 5.83)
Palpable mass	1.17 (0.52 to 2.64)	0.56 (0.20 to 1.62)	0.54 (0.16 to 1.79)
Left-sided location of the intussusceptum	7.77 (2.51 to 24.05)	3.33 (0.79 to 14.01)	3.35 (0.61 to 18.33)
Unfavorable ultrasound signs	9.35 (3.87 to 22.64)	8.92 (3.28 to 24.25)	6.83 (2.04 to 22.89)
Anemia (HCT \leq 30%)*	4.25 (1.63 to 11.05)	–	1.44 (0.36 to 5.83)
Hyponatremia (serum sodium <136 mmol/L)*	3.12 (1.28 to 7.62)	–	2.21 (0.64 to 7.64)
Hypokalemia (serum potassium <3.4 mmol/L)*	5.26 (1.65 to 16.84)	–	1.04 (0.20 to 5.40)

*New candidate item.

CMUI, Chiang Mai University Intussusception; HCT, hematocrit.

Rogers score in calculating the risk of venous thromboembolism.¹³ The prediction algorithms of these scores use multiple factors, each of which may carry varying degrees of outcome association in different settings. In

intussusception, outcome prediction was first proposed in a highly cited series consisting of 6396 cases from China in 1986. Although the fundamental properties of the scoring system were not described in their paper, the

Table 3 Analysis of additional factors associated with failure of non-surgical treatment

Parameter	All cases (n: 151)	Success group (n: 120)	Failure group (n: 31)	P value
<i>Hematologic parameters*</i>				
Hematocrit (%)				<0.01
≤30	23 (17.7%)	12 (52.2%)	11 (47.8%)	
>30	107 (82.3%)	88 (82.2%)	19 (17.8%)	
White cell count				0.61
<x10 ⁹ /L	35 (26.9%)	28 (80.0%)	7 (20.0%)	
≥x10 ⁹ /L	95 (73.1%)	72 (75.8%)	23 (24.2%)	
<i>Serum electrolytes†</i>				
Sodium (mmol/L)				0.01
<136	57 (48.3%)	37 (64.9%)	20 (35.1%)	
≥136	61 (51.7%)	52 (85.3%)	9 (14.6%)	
Potassium (mmol/L)				<0.01
<3.4	14 (11.9%)	6 (42.9%)	8 (57.1%)	
≥3.4	104 (88.1%)	83 (79.8%)	21 (20.2%)	
Chloride (mmol/L)				0.11
<98	25 (21.4%)	16 (64.0%)	9 (36/0%)	
≥98	92 (78.6%)	73 (79.4%)	19 (20.7%)	
Total carbon dioxide (mmol/L)				0.76
<20	80 (67.8%)	61 (76.3%)	19 (23.8%)	
≥20	38 (32.2%)	28 (73.7%)	10 (26.3%)	

*Complete blood count (CBC) was performed on admission in 130 patients.

†Serum chemistry on admission in 118 patients.

Table 4 Summary of modified CMUI scoring system (high risk of failed non-operative management when score >9 points)

Items	Score (points)
Body weight ≤ 9 kg	0 or 1
Prolonged duration of symptoms (>48 hours)	0 or 1
Vomiting	0 or 2
Rectal bleeding	0 or 2
Abdominal distension	0 or 2
Fever (body temperature $>37.8^{\circ}\text{C}$)	0 or 2
Palpable mass of intussusceptum	0 or 1
Left-sided location of the intussusceptum	0 or 2
Unfavorable ultrasound signs (colonic wall thickening, trapped fluid between bowel loops, ascites, signs of small bowel obstruction and absence of color flow)	0 or 2
Hyponatremia (serum sodium <136 mmol/L)	0 or 1
Total	0–16

CMUI, Chiang Mai University Intussusception.

authors, Guo and colleagues, claimed that the rate of perforation had reduced to zero after its application.¹⁴ The scoring items in Guo's scoring system were analyzed in a series from India which had 82 patients with an attempt to use hydrostatic reduction with barium enema

in 8.6% of them and 9.7% mortality.⁹ In that report, although the authors attempted to modify the original scoring system to suit their practice, the analysis did not demonstrate any statistical correlation between the modified scoring system and their reduction outcomes.

In 2013, a stepwise logistic regression analysis of 379 patients with intussusception reported that age less than 1 year, prolonged symptoms >2 days and unfavorable ultrasound features were the factors associated with the need for operative reduction.⁶ The study explored the possibility of prereduction outcome prediction by clinical and radiological parameters in cases of infantile intussusception. A study by Khorana and colleagues in 2016 in Thailand was the first attempt at a systematic construction of a clinical score for intussusception with the aim to be used as a predictive tool for non-surgical treatment of the condition.¹¹ This current study validated the Khorana *et al* score using another set of data from a university hospital in the same country, but with different practice details. In our setting, most of the patients (nearly 70%) arrived at our institute within 48 hours of the development of acute symptoms. In addition, pneumatic reduction is considered the treatment of choice unless the patient has already developed peritonitis and all the procedures are performed with full surgical back-up. Such practices may explain the relatively high success rate of non-surgical treatment and low rate of complications in our institute. This study found that a high CMUI score (>11 points)

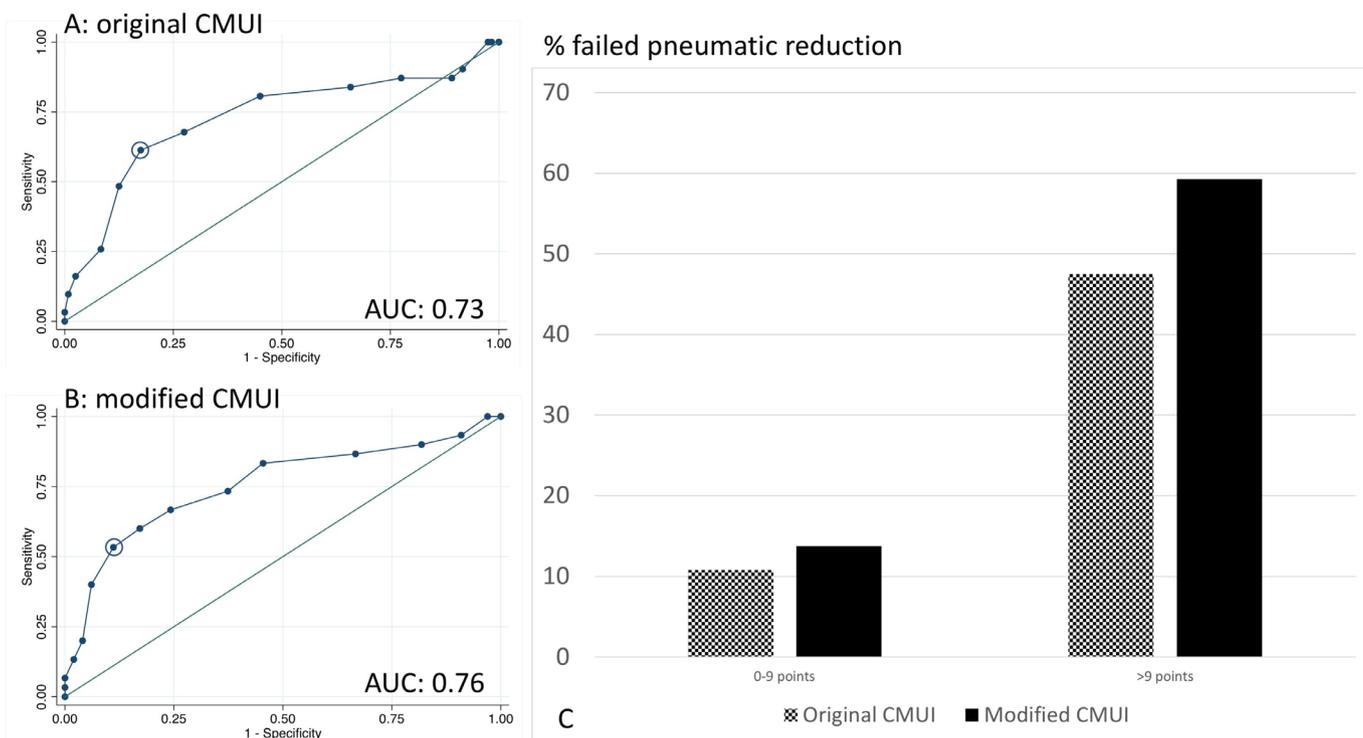


Figure 1 Receiver operating characteristic curve plots comparing sensitivity and 1-specificity of (A) the original CMUI scoring system and (B) our modified CMUI scoring system in predicting failure of pneumatic reduction of intussusception in this study; (C) percentage of cases which failed non-surgical management of intussusception in this study according to the CMUI scoring system and the modified CMUI scoring system. AUC, area under the receiver operating characteristic curve; CMUI, Chiang Mai University Intussusception.

successfully identified those patients with a significantly higher likelihood of failure of non-surgical management of intussusception at an OR of 3.57 or positive predictive value (PPV) of 44.4. Although this PPV is not high enough to contraindicate non-surgical management, the score can be valuable in suggesting more intensive surgical preparation.

In this study, we modified the CMUI scoring system by replacing the method of reduction item with another investigative item, the presence of hyponatremia. This item was chosen from investigative factors identified in our study that were shown to have significant associations with the failure of non-surgical treatment for intussusception. Although anemia (hematocrit <30%) had a stronger association, this parameter was not chosen because it was a covariate of rectal bleeding. Hyponatremia caused by intestinal loss of fluid is a common electrolyte disorder in a patient with intestinal obstruction. The main pathophysiology of hyponatremia in obstructing the intestine is a result of increased transcapillary diffusion of sodium and water into the interstitial and intraluminal spaces when the normal intestinal absorption becomes dysfunctional. Vomiting and mucous bloody diarrhea potentiate total body sodium loss.¹⁵ If the obstruction is prolonged, hyponatremia induces hyperaldosteronism and hypochloremia, which potentially leads to hypokalemia.¹⁵ In our study, hypokalemia was also associated with a higher incidence of non-surgical management failure, although with a smaller OR. After our modification, the area under the ROC curve improved from the original version although it was not higher than the figure reported in previous series that CMUI originated. In addition, our study demonstrated a stronger association and improved prediction sensitivity of the modified score when compared with the original CMUI scoring system.

The main limitation of our study was the fact that the data used in our parameter discovery set were the same as the test set for the modified scoring system. To evaluate the validity of the modified scoring system, validation in another population that uses a similar clinical strategy for choosing non-surgical treatment first is necessary.

In conclusion, this study validated the CMUI scoring system for non-surgical treatment of intussusception, and then created and validated a slightly modified version. The study suggests that either the CMUI scoring system or its modified version can be used as a risk indicator of failed non-surgical reduction. However, in the setting that exclusively uses pneumatic reduction, the latter might be more applicable.

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Contributors KB (first author and the principal investigator) pursued all data collection and analysis. SK pursued radiologic data collection and interpretation. PC pursued a part of clinical data collection and interpretation. SS (corresponding author) performed data analysis, and edited the proposal and final draft of the manuscript.

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