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ORIGINAL RESEARCH

Developing a Nomogram for Predicting Surgical Intervention in Pediatric Intussusception After Pneumatic Reduction: A Multicenter Study from China

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Purpose: The objective of this study was to develop and validate a nomogram for predicting the need for surgical intervention in pediatric intussusception after pneumatic reduction.

Patients and Methods: This retrospective study analyzed the clinical data of children with acute intussusception admitted to four hospitals in China from January 2019 to January 2022. Based on the results of pneumatic reduction, the patients were divided into two groups: the successful reduction group (control group) and the failed reduction group (operation group). The total sample was randomly divided into a training set and a validation set in a 7:3 ratio. Logistic regression analysis was performed to establish a predictive model for surgical risk.

Results: A total of 1041 samples were included in this study, with 852 in the control group and 189 in the operation group. Among the total sample, 728 cases were used for training and 313 cases were used for validation. Logistic regression analysis of the training set identified age, time of abdominal pain, presence or absence of hematostoecia, C-reactive protein value from blood test on admission, and nested position indicated by B-ultrasound as independent predictors of intussusception intervention. Based on the five independent risk factors identified through multivariate logistic regression, a nomogram was successfully constructed to predict the failure of resetting by air enema under X-ray.

Conclusion: A nomogram was developed to predict the need for surgical intervention after intussusception pneumatic reduction in children. The nomogram was based on clinical risk factors including age, time of abdominal pain, presence or absence of blood in stool, value of C-reactive protein in blood test on admission, and nested position indicated by B-ultrasound. Our internal validation demonstrated that this nomogram can serve as a useful tool for identifying risk factors associated with failure of air enema in children with intussusception.

Keywords: pediatric, intussusception, pneumatic reduction, nomogram, surgical intervention

Introduction

Acute intussusception is a common abdominal emergency in children under 2 years of age, second only to acute appendicitis.[1–3] The most common type is ileocecal junction intussusception.[4,5] Most cases are primary intussusception,

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which can easily recur and result in intestinal obstruction or necrosis.[6] In clinical practice, the main treatment methods are pneumatic reduction under X-ray fluoroscopy and water enema under ultrasound guidance.[7] However, the high cost of disposable water enema equipment poses a significant economic burden in developing countries, limiting its clinical application in China.[8,9] Consequently, most medical institutions still rely on air enema as the primary technique, which has a high success rate, good prognosis, and few complications.[10,11] In some cases, emergency surgical reduction is necessary when children fail to respond to other treatments.[5,12] Therefore, it is important to analyze the risk factors for the success of pneumatic reduction in children with intussusception and develop a clinical prediction model for identifying cases that may require surgical intervention.

Numerous studies have been conducted on intussusception reduction.[13–15] The earliest and most well-established method is the application of pneumatic reduction technology based on X-ray fluoroscopy. However, there is still a lack of standardized operating guidelines and the success rate of resetting varies.[16,17] Additionally, the evaluation of prediction models is not comprehensive enough, with most studies being conducted in single-center settings.[18–20] In this study, we conducted a retrospective analysis of the operational experience and process of pneumatic reduction in children's surgery centers at four large tertiary hospitals in China. We combined air enema parameters with general clinical information of children to develop a prediction model for rectification failure. The prediction model was comprehensively evaluated through differentiation analysis, calibration, clinical applicability, and rationality. The findings of this study aim to provide a reference and basis for the standardized application of air enema in children with emergency intussusception.

Patients and Methods

Patients

This retrospective study analyzed the clinical data of children (<14 years old) with acute intussusceptions who were hospitalized in four different hospitals: Yijishan Hospital of Wannan Medical College, Hubei Women and Children's Hospital, Guangxi Zhuang Autonomous Region Maternal and Child Health Hospital, and Qingdao Women and Children's Medical Center. The study period was from January 2019 to January 2022. All the children were diagnosed with acute intussusception through abdominal ultrasound performed by senior pediatric specialist imaging experts during their hospital visit. Senior pediatric surgeons completed the pneumatic reduction procedure, and if the reduction failed, surgical treatment was chosen (The reduction failure we refer to is defined as if the first pneumatic reduction is unsuccessful, we will try again after 30 minutes to perform the pneumatic reduction, and if it fails twice, we will choose surgery). The operating surgeons were experienced in intussusception surgery. The study collected clinical data of the children, including personal information, onset time, test results, and surgical information. Patients with short-term relapses and those with incomplete medical records were excluded from the study. Based on the results of pneumatic reduction, the children were divided into two groups: the successful reduction group (control group) and the failed reduction group (operation group). The study received approval from the Ethics Committee of Yijishan Hospital, Wannan Medical College (No. 2023-LSYD-24), and written consent was obtained from the parents of the patients.

Pneumatic Reduction

Pneumatic reduction was performed using the Jinjian medical computer remote control enema rectification instrument (JS-628E) manufactured by Guangzhou Jinjian Medical Equipment Co., LTD. This instrument is approved by the Guangdong Food and Drug Administration (quasi-) word 2010 No. 2540666, China. The machine provides real-time display of the working pressure, setting pressure, and safety pressure. The safety pressure is set at 12kPa, with a power consumption of 50 VA and dimensions of 490×470 × 1130 mm. For this study, the initial pressure value of the air enema machine was set at 6kPa, with the option to increase it by 0.5kPa increments. The critical pressure value was set at 10kPa, and the maximum allowed pressure was 12kPa. If the pressure exceeded 12kPa, the machine would automatically sound an alarm to prevent intestinal perforation caused by overinflation.

Data Collection

The total sample of patients enrolled in this study was randomly divided into a training set and a validation set in a 7:3 ratio. The training set was primarily used to train the prediction model, while the validation set was used to verify the validation model.

Statistical Method

SPSS 26.0 and R 4.2.0 were utilized to analyze the data. Baseline data were automatically identified and analyzed using the compare-groups package. Frequency and percentage were used to represent counting data, while median and interquartile interval were used for measurement data. Single factor variable screening was conducted using logistic regression, followed by multi-factor logistic regression analysis. If the screening variables differed, separate models were constructed and their capabilities were compared. The model differentiation was evaluated using the receiver operating characteristic (ROC) curve, while the clinical application value was assessed using the decision curve. AUC>0.7 indicated a good model differentiation, and P>0.05 by the Hosmer Lemeshow test indicated a high model differentiation ability. Finally, a nomogram and ROC curve for each single variable were drawn to assess the model's rationality.

Results

Baseline Analysis of General Data

In this study, a total of 1108 children with acute intussusception were included. After excluding 67 children with incomplete clinical data, who had not received X-ray fluoroscopy, were transferred to another hospital, or underwent direct surgery, we finally included 1041 children. Among them, 852 were in the control group and 189 were in the operation group. The total samples were randomly divided into 728 training sets and 313 validation sets, following a 7:3 ratio (Figure 1). Among the 1041 cases, 696 were boys and 345 were girls, resulting in a male-to-female ratio of 2.02:1. The highest proportion of children belonged to the age group of 12–24 months, accounting for 24.40% (Figure 2). There were no significant differences between the control group and the operation group in four indicators: sex, body weight, temperature at admission, and white

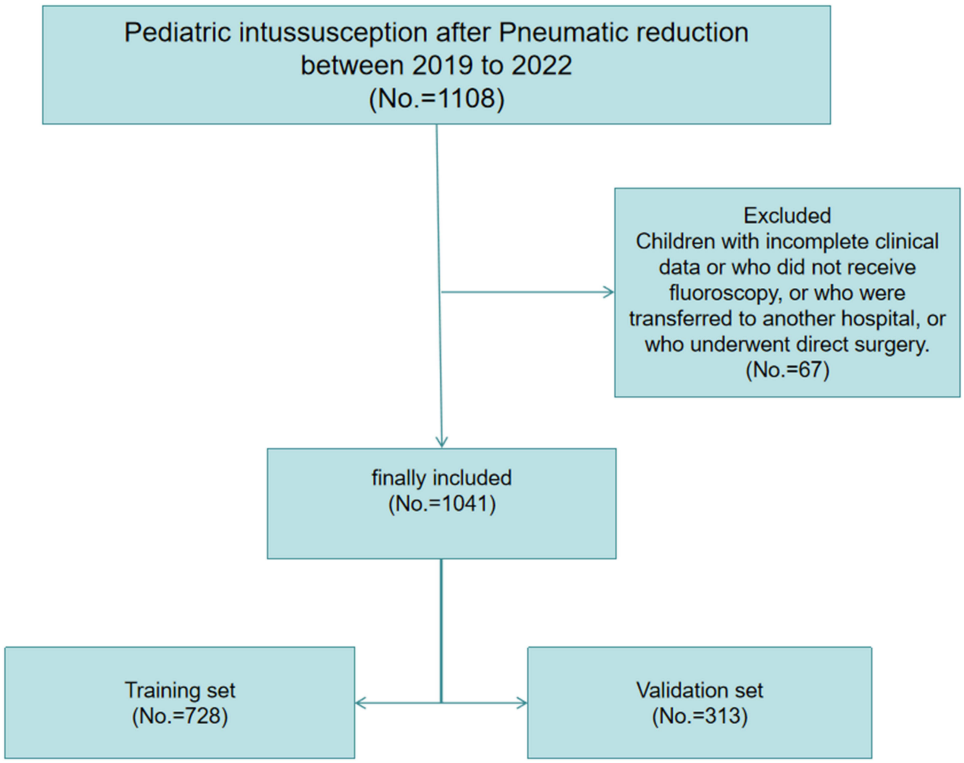

Figure 1 Study flowchart displaying the selection of patients with pediatric intussusception according to exclusion criteria.

Figure 2 Analysis of some clinical data of children with acute intussusception in this study. (**A**) Gender distribution map of children with acute intussusception in this study. (**B**) Age (Months) histogram of children with acute intussusception in this study. (**C**) Age (Months) histogram of children with acute intussusception in the successful reduction group (control group) of this study. (**D**) Age (Months) histogram of children with acute intussusception in the failed reduction group (operation group) of this study.

blood cell count in blood routine examination at admission (P>0.05). However, there were statistical differences in five indicators between the two groups: age, time of abdominal pain, presence or absence of blood stool, value of C-reactive protein detected at admission, and nested position indicated by B-ultrasound (P<0.05) (Table 1). There was no statistical difference in the above indexes between the two groups in the training set and the validation set (P>0.05) (Table 2).

Single Factor and Multi-Factor Analysis

The results of the univariate logistic regression analysis revealed that there were no statistically significant differences in four indexes, sex, body weight, temperature at admission, and white blood cell count in the blood routine examination at admission. However, there were statistically significant differences in age, abdominal pain time, blood in stool, C-reactive protein value in the blood test at admission, and the nested position indicated by B-ultrasound (P<0.05). Subsequently, a multivariate logistic regression analysis was conducted on the variables identified through the univariate logistic regression. The results indicated that age, time of abdominal pain, presence or absence of hematochezia, the value of C-reactive protein in the blood test at admission, and the nested position indicated by B-ultrasound were statistically significant (P<0.05) (Table 3). Finally, five independent risk factors were selected for model construction.

Development of the Nomogram

The ROC curve demonstrated that the model effectively differentiated the risk of failure in predicting enterointussusception air rectifying in children (Figure 3A and B). The training set AUC was 0.757 (95% CI: 0.703~0.812), while the validation set AUC

Table 1 Demographic and Clinical Characteristics Children with Intussusception

Characteristics	Control Group	OR Group	t (x^2) value	P value
No.	852	189		
Sex			2.710	0.100
Boys	560 (65.7%)	136 (72%)		
Girls	292 (34.3%)	53 (28%)		
Age (Mo.)	33.50±20.98	26.55±27.56	3.266	0.001
Weight, mean ± SD (Kg)	12.27±3.78	11.87±5.52	0.959	0.339
Abdominal pain time (h)	16.87±18.46	24.20±31.03	−3.124	0.002
Hematochezia (1=Yes, 0=No)			222.02	< 0.001
1	90 (10.6%)	109 (57.7%)		
0	762 (89.4%)	80 (42.3%)		
Temperature (°C)	36.79±0.49	36.80±0.54	−0.285	0.776
WBCs, $\times 10^9$/L	11.36±4.52	10.79±5.01	1.529	0.127
CRP (mg/L)	7.23±7.31	10.75±17.43	−2.725	0.007
Nested position (Right colon=1, Left colon=2, No.)			31.223	< 0.001
1	698 (81.9%)	120 (63.5%)		
2	154 (18.1%)	69 (36.5%)		

Abbreviations: Control Group, successful reduction group; OR Group, failed reduction group (operation group); OR, operation; WBC, white blood cell; CRP, C-reactive protein.

Table 2 Baseline Comparison of Validation Set and Training Set

Characteristics	Training Set	Validation Set	P value
No.	728	313	
Sex			0.210
Boys	478 (65.66%)	218 (69.65%)	
Girls	250 (34.34%)	95 (30.35%)	
Age (Mo.)	32.05 ± 22.56	32.69 ± 22.27	0.527
Weight, mean ± SD (Kg)	12.21 ± 4.16	12.18 ± 4.14	0.832
Abdominal pain time (h)	17.67 ± 20.07	19.45 ± 24.42	0.3242
Hematochezia (1=Yes, 0=No)			0.375
1	134 (18.41%)	65 (20.77%)	
0	594 (81.59%)	248 (79.23%)	
Temperature (°C)	36.8 ± 0.5	36.79 ± 0.5	0.5492
WBCs, $\times 10^9$/L	11.23 ± 4.7	11.3 ± 4.44	0.5612
CRP (mg/L)	7.9 ± 10.35	7.8 ± 9.23	0.614
Nested position (Right colon=1, Left colon=2, No.)			0.185
1	564 (77.47%)	254 (81.15%)	
2	164 (22.53%)	59 (18.85%)	

Abbreviations: WBC, white blood cell; CRP, C-reactive protein.

was 0.712 (95% CI: 0.610~0.814). Moreover, the calibration curve indicated that the model accurately predicted the risk of failure of intussusception air enema, as it aligned well with the actual situation (Figure 3C and D). Additionally, the decision curve analysis (DCA) demonstrated the model's clinical applicability across a wide range of probability values (Figure 4A and B). Based on multivariate logistic regression, we identified 5 independent risk factors. Using these factors, we successfully constructed a nomogram for predicting the failure of pneumatic reduction under X-ray monitoring (Figure 5). Each predictive factor corresponds to a specific score criterion, and the total score is calculated at the bottom to determine the predicted probability of pneumatic reduction failure.

Table 3 Univariate and Multivariate Logistic Regression Results

Characteristics	Univariate Analysis		Multivariate Analysis	
	Odds Ratio (95% CI)	P value	Odds Ratio (95% CI)	P value
Sex	1.338 (0.945–1.894)	0.101	–	–
Age (Mo.)	0.984 (0.976–0.992)	< 0.001	0.980 (0.966–0.994)	0.006
Weight (Kg)	0.976 (0.937–1.015)	0.226	-	–
Abdominal pain time (h)	1.013 (1.006–1.019)	< 0.001	1.016 (1.008–1.024)	< 0.001
Hematochezia	0.087 (0.060–0.124)	< 0.001	0.092 (0.060–0.141)	< 0.001
Temperature (°C)	1.049 (0.770–1.431)	0.761	–	–
WBCs, ×109/L	0.973 (0.938–1.008)	0.127	–	–
CRP (mg/L)	1.029 (1.014–1.043)	< 0.001	1.034 (1.016–1.052)	< 0.001
Nested position	0.384 (0.272–0.541)	< 0.001	0.600 (0.390–0.924)	0.020

Abbreviations: WBC, white blood cell; CRP, C-reactive protein.

Discussion

In this study, we have developed and validated a comprehensive nomogram for predicting the probability of surgical intervention in children with intussusception, based on clinical risk factors. The nomogram incorporates factors such as age, duration of abdominal pain, presence of blood in stool, C-reactive protein levels in blood test, and nested position indicated by B-ultrasound. The training set analysis demonstrated the inclusion of these risk factors in the nomogram. In the validation set, our study confirms that the nomogram is a highly predictive tool that can be directly applied.

Nomograms are widely recognized as valuable prognostic tools in medicine as they integrate various prognostic and determining variables to generate individual probabilities of clinical events.[21,22] However, there is a scarcity of reports on nomogram prediction models for intussusception, with most studies being single-center studies. For instance, Ting et al[18] conducted a study with 368 patients undergoing intussusception surgery and developed a nomogram to predict pathological intussusception in children. They identified timing of onset, mass length, and history of infection as independent predictors. Similarly, Zhuang et al[19] retrospectively analyzed clinical data from 139 children who underwent hydrostatic reduction for intussusception and developed a preoperative nomogram using multiple logistic regression analysis. Their study identified several effective predictors including duration of symptoms, presence of blood in stool, white blood cells count, CK-MB levels, long axis diameter, ultrasound findings indicating adverse prognosis, and mental state of the children. In contrast, our study is a large-scale, multicenter study that includes data from four major children's medical centers in Anhui, Hubei, Guangxi Zhuang Autonomous Region, and Shandong provinces of China. To the best of our knowledge, this is the first study of its kind to develop a nomogram specifically for pediatric intussusception surgery interventions.

Fallon et al and Tota-Maharaj et al discovered that children under the age of 1 year were significantly more likely to experience failure in reduction.[23,24] Kim et al,[25] in a systematic review and meta-analysis of predictors of enema failure in children with intussusception, also identified being younger than 1 year as a cause of failure. The column chart in their study reveals that as the age of children decreases, the likelihood of failure increases. The age cut-off value for failure is 13.5 months, which aligns with previous research.[8] Our analysis suggests that this may be due to incomplete intestinal wall function in young children.

The relationship between disease duration and enema success has been a topic of debate. Xie et al[26] considered symptom duration of 48 hours or more as a risk factor for hydrostatic reduction failure in intussusception. Khorana et al[27] identified symptom duration exceeding 72 hours as a predictor of non-surgical reduction failure. However, Lim et al's[28] retrospective study, conducted at a tertiary referral center in Malaysia, found no correlation between symptom duration, clinical manifestations such as blood in the stool and vomiting, and the success of ultrasound-guided enterointussusception water enema in children. Liu et al[29] also concluded that there was no statistical difference in the success rate of ultrasound-guided hydrostatic enema between children with a disease duration of more than 48 hours and those with a duration of less than 48 hours. Our study indicates that a longer duration of abdominal pain (with a cut-off value of 24.5

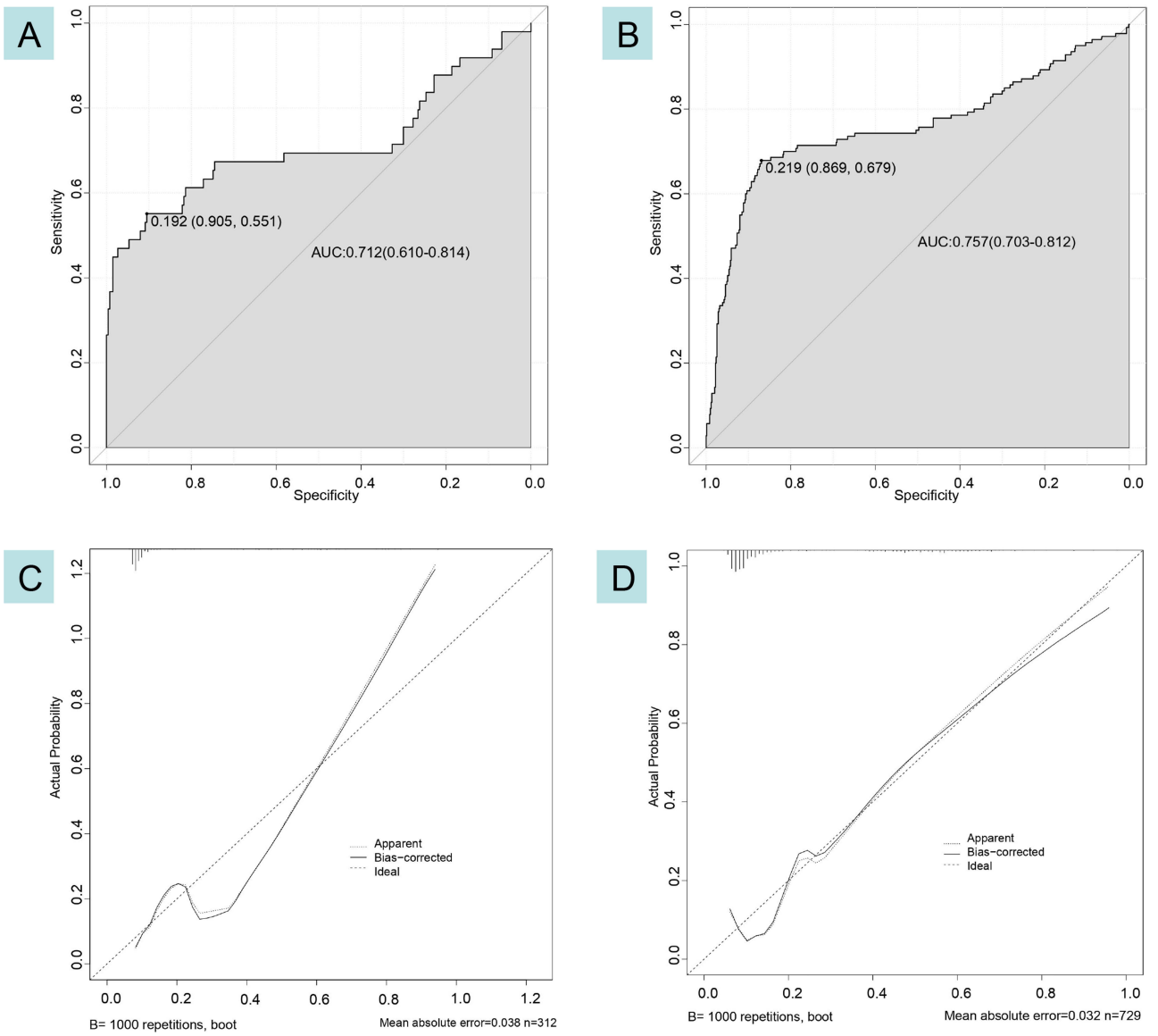

Figure 3 Distinguishing ROC curve and calibration curve of risk prediction model for intussusception failure. (**A**) ROC curve in training set. (**B**) ROC curve in validation set. (**C**) Calibration curve of the model in the training set. The Y-axis represents the actual surgical intervention rate. The x-axis represents the predicted risk of surgical intervention. The dotted line represents a perfect prediction by an ideal model. (**D**) Calibration curve of the model in the validation set. The Y-axis represents the actual surgical intervention rate. The x-axis represents the predicted risk of surgical intervention. The dotted line represents a perfect prediction by an ideal model.
Abbreviations: ROC, receiver operating characteristic; AUC, area under the curve.

hours) is a risk factor for enema failure, meaning that children with a duration exceeding 24.5 hours are more likely to require surgery. Furthermore, our study confirms that the presence of blood in the stool is also a risk factor, consistent with previous research.[19]

The study participants in this research were children who had been hospitalized, and a significant amount of blood test data was collected. Our study is the first to demonstrate that C-reactive protein can be used as an independent predictor for intervention in intussusception cases. In contrast, the leukocyte count may not be considered as an independent risk factor. This finding contradicts the results of Zhuang et al's study,[19] in which white blood cell count was found to be an independent risk factor but C-reactive protein was not. Chen et al's[30] study also confirmed that in cases of intussusception in children, the C-reactive protein levels were significantly higher in patients who underwent enterectomy compared to those who did not. This suggests that C-reactive protein levels may be a more accurate indicator of inflammation compared to white blood cells. Khorana et al[27] suggested that body weight is a factor that affects the success of enema,

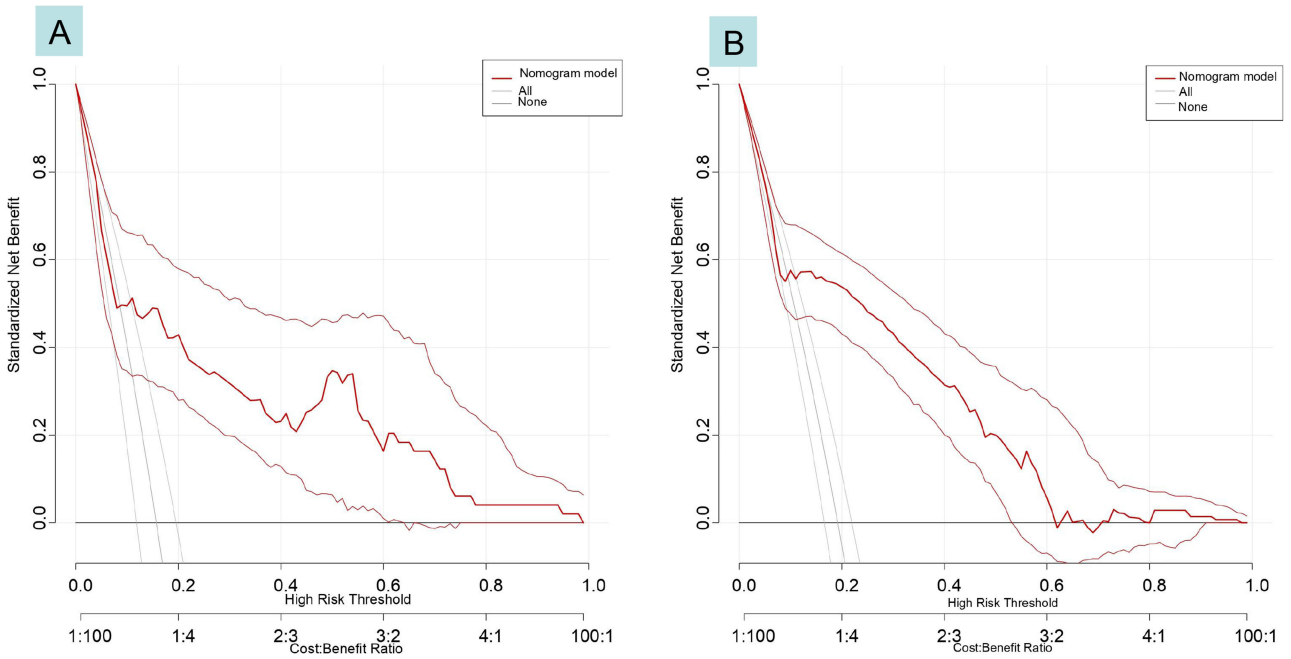

Figure 4 Decision curve analysis (DCA) for the predictive model. The net benefit was produced against the high-risk threshold. The red line represents the predictive model. The application of this predictive model would add net benefit compared with either the treat-all or the treat-none strategies. (**A**) DCA in training set; (**B**) DCA in validation set.

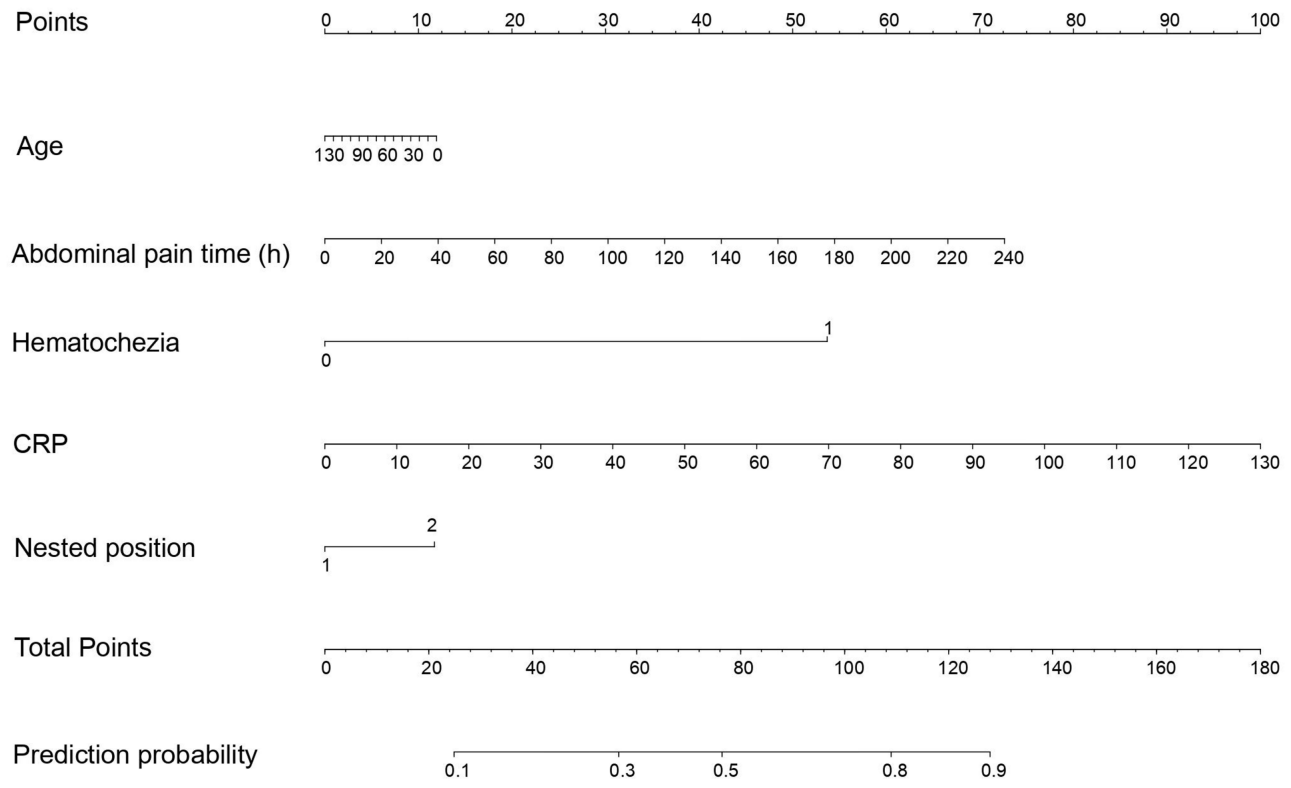

Figure 5 The nomogram for predicting the risk of surgical intervention in pediatric intussusception after pneumatic reduction. The nomogram is based on clinical risk factors, including age, time of abdominal pain, presence or absence of blood in stool, value of C-reactive protein in blood test on admission, and nested position indicated by B-ultrasound, etc. Different levels of each variable correspond to the top score Points. Individual Points and Total Points. Finally, the Prediction probability of risk can be calculated.

with children weighing less than 12 kg being more likely to fail. However, our study found that body weight is not a reliable predictor, and it is possible that our larger sample size helped reduce bias in the analysis.

This retrospective study had limitations as it did not consider other potential predictors. Moreover, China's diverse population, vast land area, and varying climates and eating habits were not taken into account in the sample analysis. The study also did not analyze the children's living environment and other factors. Future studies are encouraged to develop a multi-scale prediction model using data from multiple centers, larger samples, and different modes to externally validate and enhance the model's robustness and clinical applicability. In addition, this study included all pediatric patient who diagnosed with acute intussusception, both primary and secondary type. Secondary type also called pathological intussusception, we did not excluded in the study and not analyzed as an independent factor which may lead to a bias to the other factors. We are conducting a separate study on risk prediction models for secondary intussusception in cases requiring surgery, and have completed preliminary data collection and analysis.

Conclusions

In conclusion, this study aimed to develop a nomogram using clinical risk factors to predict the need for surgical intervention following intussusception pneumatic reduction in children. The predictors included in the nomogram were age, duration of abdominal pain, presence or absence of blood in stool, C-reactive protein levels in blood test upon admission, and nested position indicated by B-ultrasound. The internal validation of our study demonstrates that this nomogram can serve as a helpful tool for identifying risk factors associated with the failure of air enema in children with intussusception.

Data Sharing Statement

The original contributions generated for the study are included in the article, further inquiries can be directed to the corresponding author/s.

Ethics Approval and Consent to Participate

The present study was in accordance with the Declaration of Helsinki and was approved by the Ethics Committee of Yijishan Hospital of Wannan Medical College (No. 2023-LSYD-24), and all the legal guardians of children involved in this study signed the informed consent form.

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Author Contributions

All authors have approved the final version of the manuscript. JL, YW and ZJ contributed equally to this paper. JL, YW and DZ designed the research, analyzed the data, and wrote the manuscript; XM, GD, and ZJ analyzed and interpreted the data; JL, YW and ZJ designed the research, analyzed the data, and corrected the manuscript. All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas, took part in drafting, revising or critically reviewing the article, gave final approval of the version to be published, have agreed on the journal to which the article has been submitted, and agree to be accountable for all aspects of the work.

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Disclosure

The authors report no competing interests in this work.

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