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# Developing a nomogram to predict recurrent intussusception after pneumatic reduction of primary intussusception in children

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## Abstract

**Background** Intussusception is a common acute abdominal disease in children, often leading to acute ileus in infants and young children.

**Objective** This study aimed to develop and validate a nomogram for predicting recurrent intussusception in children within 48 h after pneumatic reduction of primary intussusception.

**Methods** Clinical data of children with acute intussusception admitted to multiple hospitals from March 2019 to March 2021 were retrospectively analyzed. The children were divided into a successful reduction control group (control group) and a recurrent intussusception group (RI group) according to the results of pneumatic reduction.

**Results** A total of 2406 cases were included in this study, including 2198 control group and 208 RI group. In the total sample, 1684 cases were trained and 722 cases were verified. A logistic regression analysis was conducted to establish a predictive model based on age, abdominal pain time, white blood cells count, and hypersensitive C-reactive protein levels as independent predictors of intussusception recurrence. The nomogram successfully predicted recurrent intussusception after pneumatic reduction.

**Conclusion** In this study, a nomogram was developed based on clinical risk factors to predict recurrent intussusception following pneumatic reduction in children. Age, abdominal pain time, white blood cell counts, and hypersensitive C-reactive protein levels were identified as predictors and incorporated into the nomogram. Internal validation demonstrated that this nomogram can offer a clear and convenient tool for identifying risk factors for recurrence of intussusception in children undergoing pneumatic reduction.

**Keywords** Pediatric, Recurrent intussusception, Pneumatic reduction, Nomogram, Predicting

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## Introduction

Intussusception is a common acute abdominal disease in children, often leading to acute ileus in infants and young children [1, 2]. It can be categorized into primary and secondary types, with primary cases comprising over 95% of occurrences in children [3, 4]. Untreated cases may result in severe complications such as intestinal necrosis, perforation, peritonitis, and even death due to reduced blood supply to the intestines [5, 6]. In China, due to the high cost of ultrasound-guided hydrostatic reduction, pneumatic reduction is the primary treatment for initial intussusception in children, with a success rate exceeding 90% [7, 8]. However, recurrent intussusception (RI) shortly after reduction poses a significant challenge, potentially leading to serious complications if not promptly addressed [9, 10]. The underlying cause of recurrence in children remains poorly understood, hindering accurate prediction of RI [11].

Despite existing reports on risk factors for RI in children post-reduction, a lack of consensus persists [12]. Many studies are limited in scope or are predominantly single-center, with some results even yielding conflicting conclusions [12, 13]. To better predict the likelihood of RI in children and minimize treatment risks, this study retrospectively analyzed clinical data from pneumatic reduction procedures at six major tertiary hospitals in China. A predictive model was developed to assess the risk of RI, aiming to offer guidance for timely treatment following reduction.

## Materials and methods

### Patients

This study retrospectively analyzed the clinical data of acute intussusception in children (<14 years old) who were initially treated with pneumatic reduction at Yi Jishan Hospital of Wannan Medical College (Anhui Province), Hubei Maternal and Child Health Care Hospital (Hubei Province), Wuhan Children's Hospital of Hubei Province (Hubei Province), Maternal and Child Health Hospital of Guangxi Zhuang Autonomous Region (Guangxi Zhuang Autonomous Region), Qingdao Women and Children's Medical Center (Shandong Province), and Affiliated Hospital of Qingdao University (Shandong Province) from March 2019 to March 2021. The children were diagnosed by senior pediatric surgeons and imaging specialists, followed by pneumatic reduction if necessary.

Indications for pneumatic reduction include patients with intussusception who are within 48 h of symptom onset, have a stable general condition, exhibit no signs of peritonitis, and show no significant symptoms of dehydration or shock. Conversely, contraindications for pneumatic reduction encompass patients with intussusception lasting longer than 48 h, those in poor general condition,

individuals presenting with fever, dehydration, or shock, patients displaying signs of peritoneal irritation, those with suspected intestinal necrosis, patients with small intestinal intussusception, and individuals exhibiting significant abdominal distension along with large fluid levels on abdominal imaging. Patients with RI within 48 h underwent emergency abdominal ultrasound and repeat pneumatic reduction if needed. To reduce study bias, patients with ileal intussusception were excluded from this study. Detailed clinical information was collected and patients were divided into successful reduction group (control group) and RI group. The study focused on children with short-term recurrence, excluding those requiring surgery, with secondary intussusception, recurrence longer than 48 h, and those lost to follow-up after pneumatic reduction. Ethics approval was obtained from Yijishan Hospital, Wannan Medical College (No. 2022–105), with parental consent.

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

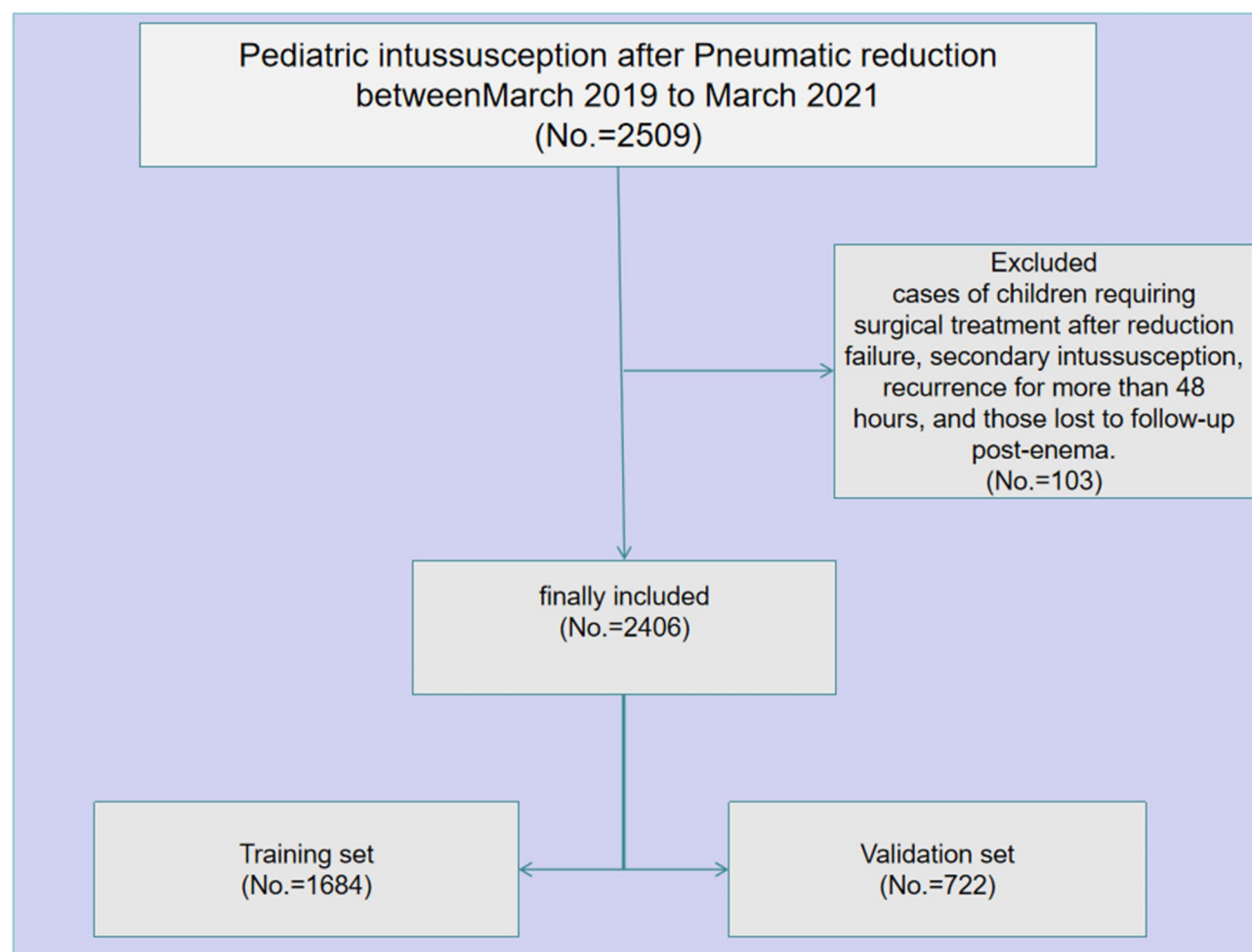
### Statistical method

Data processing and analysis were performed using R version 4.3.0 (2023-04-21), along with Storm Statistical Platform ([www.medsta.cn/software](http://www.medsta.cn/software)). Receiver Operating Characteristic (ROC) curve was used to evaluate model differentiation, and decision curve was used to evaluate clinical application value.  $AUC > 0.7$  indicated good model differentiation, and  $P > 0.05$  in Hosmer Lemeshow test indicated high model differentiation ability. Finally, a nomogram and univariate ROC curve were drawn to observe the rationality of the model.

## Results

### Baseline analysis of general data

In this study, a total of 2509 cases of acute intussusception in children were initially collected. After excluding cases of children requiring surgical treatment after reduction failure, secondary intussusception, recurrence for more than 48 h, and those lost to follow-up post-enema, 2406 children were included in the study. This cohort comprised 2198 cases in the control group and 208 cases in the RI group (Fig. 1.). Among the 2406 children, 1620 were boys and 786 were girls, resulting in a male to female ratio of 2.06:1. The total samples were randomly divided into 1684 training sets and 722 verification sets at a 7:3 ratio. Statistical analysis revealed no significant differences between the control group and the RI group in both the training and verification sets ( $P > 0.05$ ) (Table 1).



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

**Table 1** Baseline comparison of validation set and training set

Variable	Total (n = 2406)	train_set (n = 1684)	valid_set (n = 722)	Statistic	P
Age (Mo.), Mean $\pm$ SD	30.12 $\pm$ 19.97	30.50 $\pm$ 20.26	29.24 $\pm$ 19.26	t = 1.415	0.157
Weight (Kg), Mean $\pm$ SD	12.69 $\pm$ 3.94	12.78 $\pm$ 4.03	12.46 $\pm$ 3.69	t = 1.914	0.056
Abdominal Pain time (h), Mean $\pm$ SD	15.31 $\pm$ 12.80	15.03 $\pm$ 12.67	15.96 $\pm$ 13.06	t = -1.629	0.103
Temperature ( $^{\circ}$ C), Mean $\pm$ SD	36.71 $\pm$ 0.49	36.71 $\pm$ 0.49	36.71 $\pm$ 0.48	t = -0.092	0.927
WBC ( $\times 10^9$ /L), Mean $\pm$ SD	10.17 $\pm$ 3.52	10.12 $\pm$ 3.54	10.29 $\pm$ 3.46	t = -1.075	0.282
hs-CRP (mg/L), Mean $\pm$ SD	7.38 $\pm$ 7.82	7.23 $\pm$ 7.58	7.71 $\pm$ 8.35	t = -1.378	0.168
Sex, n (%)				$\chi^2 = 0.088$	0.766
Boys	1620 (67.33)	1137 (67.52)	483 (66.90)		
Girls	786 (32.67)	547 (32.48)	239 (33.10)		
Hematochezia, n (%)				$\chi^2 = 0.188$	0.665
Yes	411 (17.08)	284 (16.86)	127 (17.59)		
No	1995 (82.92)	1400 (83.14)	595 (82.41)		

### Single factor and multi-factor analysis

To investigate the factors influencing intussusception recurrence, univariate logistic regression analysis was conducted. The findings revealed no statistically significant differences in sex, body weight, temperature at admission, and presence of blood in the stool ( $P > 0.05$ ).

However, age, abdominal pain time, white blood cell count, and hypersensitive C-reactive protein levels showed significant variations ( $P < 0.05$ ). Subsequently, a multivariate logistic regression analysis was performed on the variables identified in the univariate analysis, confirming significant differences in age, abdominal pain

time, white blood cell count, and hypersensitive C-reactive protein levels ( $P < 0.05$ ) (Table 2). Finally, a model was constructed using the four independent risk factors identified through multivariate logistic regression analysis.

### Development of the nomogram

The ROC curve analysis in this study demonstrated that the model effectively predicted the risk of RI following pneumatic reduction in children, as depicted in Fig. 2A and B. The Area Under Curve (AUC) for the training set was 0.911 (95% CI: 0.864–0.958), while for the validation set it was 0.926 (95% CI: 0.876–0.976). Furthermore, the calibration curve illustrated that the model's predictions aligned well with the actual outcomes regarding recurrent intussusception after air enema reduction, as shown in Fig. 2C and D. The decision curve indicated that the model had significant clinical utility across various probability thresholds, as depicted in Fig. 3A and B. To enhance the accuracy of predicting recurrent intussusception post air enema reduction, a Nomogram was developed based on four independent risk factors (age, abdominal pain time, white blood cell counts, and hypersensitive C-reactive protein levels) identified through multivariate logistic regression analysis. This Nomogram enables the prediction of recurrent intussusception risk following pneumatic reduction based on a calculated score, as illustrated in Fig. 4.

### Discussion

The potential recurrence of intussusception following the reduction of acute intussusception via enema is a concern for pediatric surgeons and parents. However, in the short term, the recurrence of intussusception may go unnoticed by medical staff due to atypical symptoms, leading to serious complications and medical risks [14, 15]. In this study, we have developed and validated a Nomogram that can accurately predict the likelihood of RI in the short term post-reduction of primary

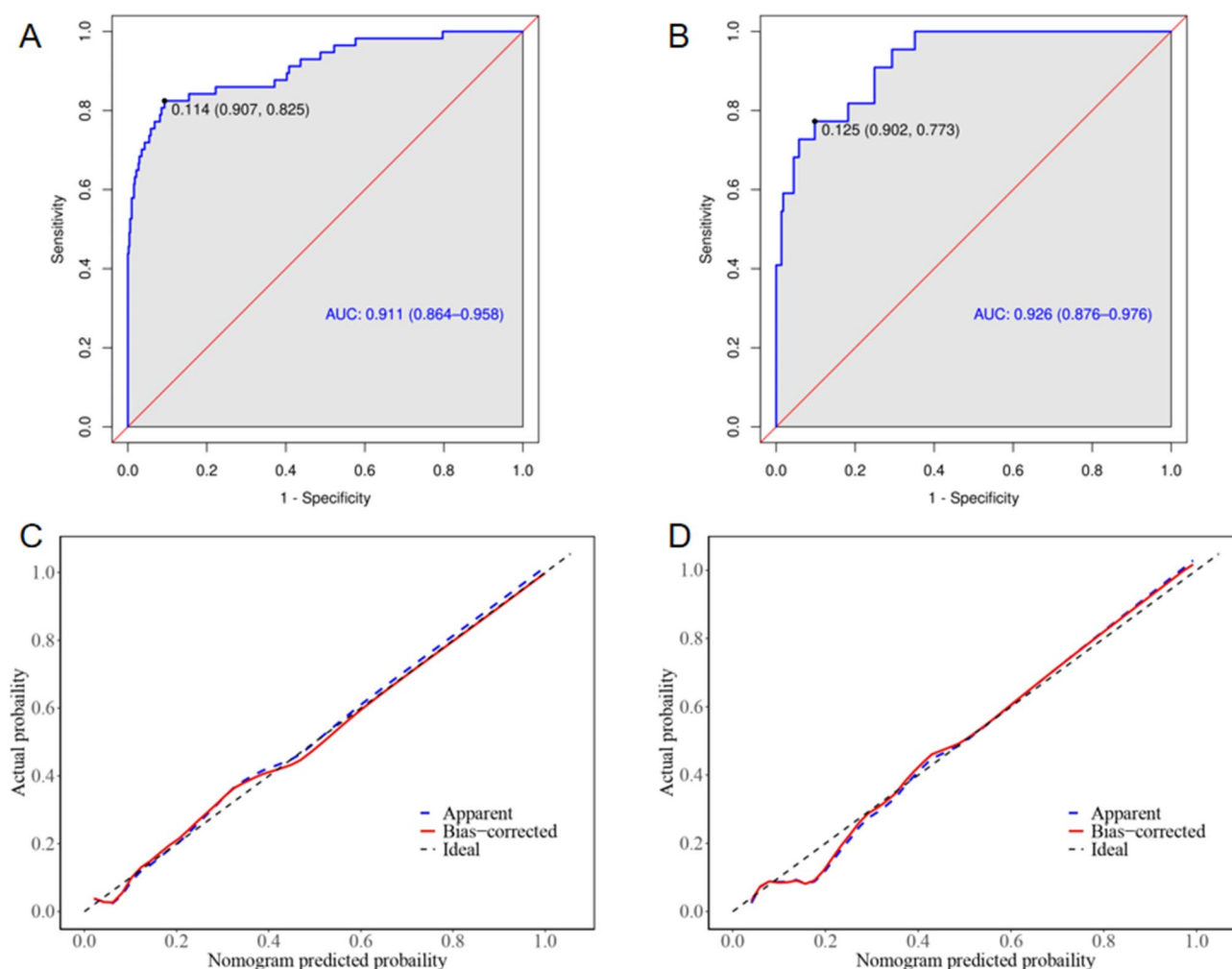
intussusception. This nomogram utilizes clinical risk factors to aid in predicting therapeutic interventions for RI in children, thereby reducing treatment risks. Our analysis of the training set revealed that age, abdominal pain time, white blood cell counts, hypersensitive C-reactive protein levels, and other risk factors were incorporated into the nomogram to successfully construct the prediction model. Furthermore, our multicentre internal validation set confirmed the model's effectiveness as a highly predictive tool for identifying recurrent intussusception following pneumatic reduction.

This multi-center study on pediatric surgery was conducted in six large tertiary hospitals in China, where the medical technology is at the forefront locally and the treatment outcomes for intussusception are positive. The statistical analysis revealed that the short-term recurrence rate of intussusception after pneumatic reduction was 8.65%, lower than the 53.1% reported by Cho et al. [16] and slightly higher than the 1.4% reported by Litz et al. [17], indicating potential regional or racial variations. Interestingly, there was no significant difference in RI between genders, aligning with the findings of a meta-analysis by Ye et al. [12]. On the contrary, Vo et al. [18] reported a retrospective study of 200 children suggesting a higher incidence of intussusception recurrence in females compared to males. It is important to note that due to the small sample size of Vo et al.'s study [18], there might be some bias in their results.

The relationship between age and RI remains a topic of debate in the literature. Kim et al. [13] and Xie et al. [19] identified being older than 2 years as a risk factor for recurrence, while Wang et al. [20] and Guo et al. [14] suggested that children over 1 year old faced a higher risk. Conversely, Vo et al. [18] reported no significant association between age and intussusception recurrence. The findings of our study indicate that age is indeed a risk factor for RI, with children older than 20.5 months being more likely to experience a recurrence. Our raw data

**Table 2** Univariate and multivariate logistic regression results

Variables	Univariable analysis					Multivariable analysis				
	Beta	S.E	Z	OR (95%CI)	P	aBeta	aS.E	aZ	aOR (95%CI)	aP
Age (Mo.)	0.01	0.00	3.11	1.01 (1.01–1.02)	0.002	0.01	0.00	2.49	1.01 (1.01–1.02)	0.013
Weight (Kg)	0.03	0.02	1.65	1.03 (0.99–1.08)	0.100					
Abdominal Pain time (h)	0.02	0.01	2.66	1.02 (1.01–1.03)	0.008	0.02	0.01	2.51	1.02 (1.01–1.03)	0.012
Temperature (°C)	0.17	0.17	1.00	1.18 (0.85–1.64)	0.317					
WBC ( $\times 10^9/L$ )	0.23	0.03	7.23	1.26 (1.18–1.33)	<0.001	0.11	0.04	3.27	1.12 (1.05–1.20)	0.001
hs-CRP (mg/L)	0.17	0.02	11.00	1.18 (1.15–1.22)	<0.001	0.15	0.02	9.15	1.16 (1.13–1.20)	<0.001
Sex										
Girls				1.00 (Reference)						
Boys	0.20	0.20	1.00	1.22 (0.83–1.81)	0.316					
Hematochezia										
No				1.00 (Reference)						
Yes	-0.03	0.24	-0.10	0.98 (0.61–1.57)	0.917					



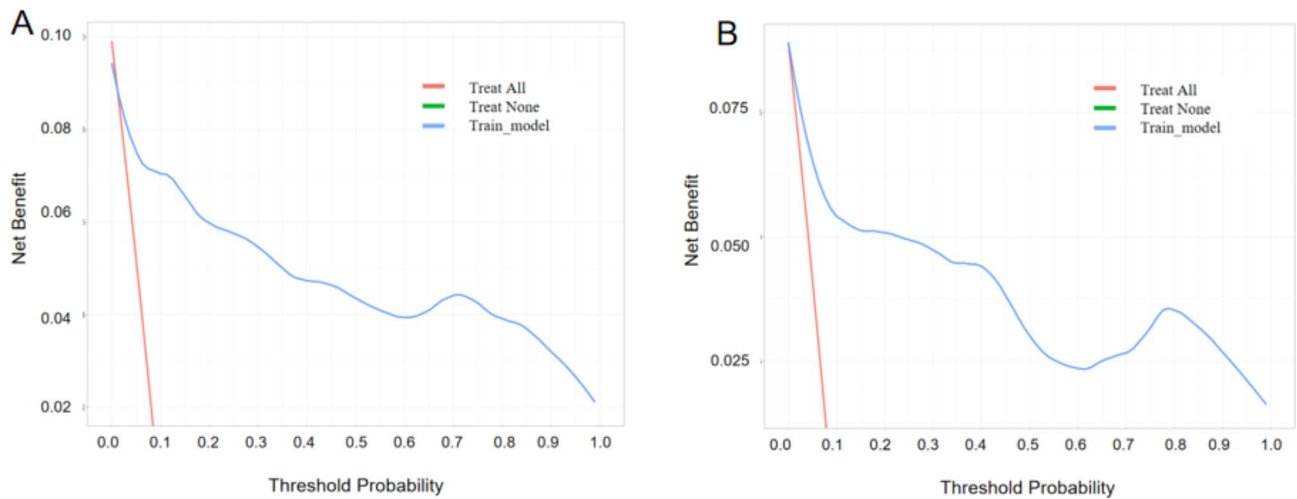
**Fig. 2** Distinguishing ROC curve and calibration curve of risk prediction model for recurrent intussusception. **(A)** ROC curve in training set. ROC, receiver operating characteristic; AUC, area under the curve. **(B)** ROC curve in validation set. ROC, receiver operating characteristic; AUC, area under the curve. **(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

were accurate to months, which provided us with more accurate data guarantee for studying the relationship between age and recurrence.

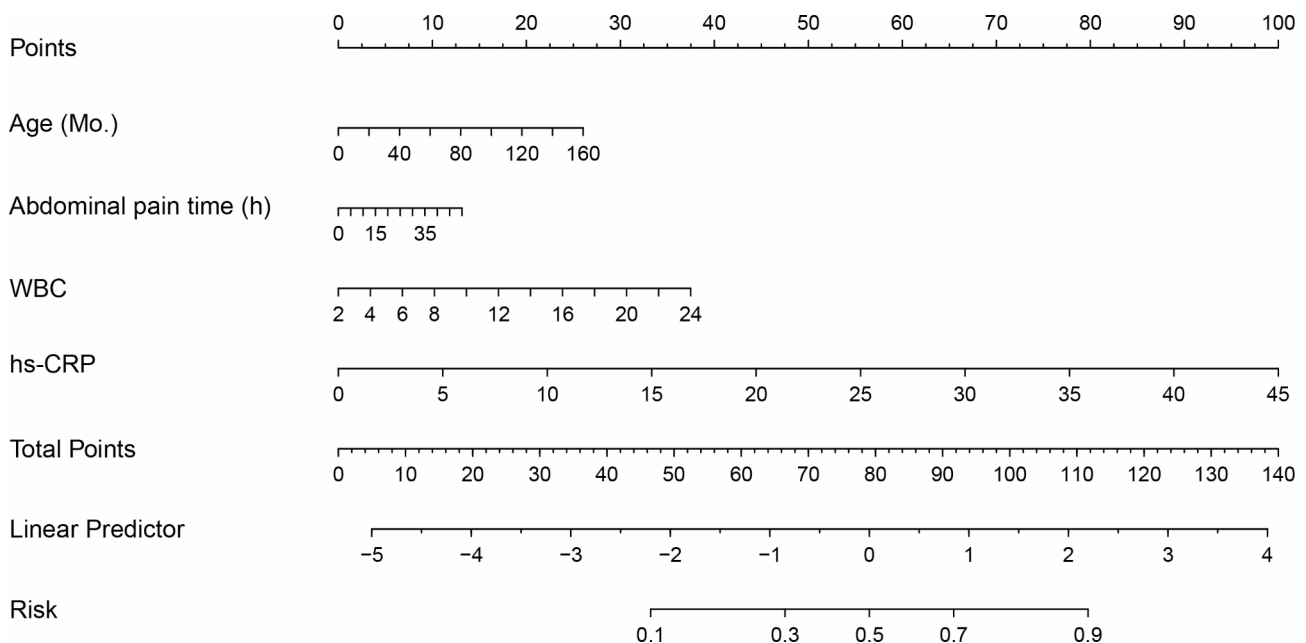
The relationship between onset time and recurrence of pneumatic reduction remains inconclusive. Xie et al. [19] identified risk factors for RI in cases with abdominal pain lasting over 48 h, while Guo et al. [14] suggested that children with abdominal pain lasting less than 12 h had a higher recurrence rate after pneumatic reduction. Some scholars, like Kim et al. [13], observed that longer duration of abdominal pain was associated with increased recurrence rate of intussusception post-enema, although statistical analysis did not show a significant difference (12.5 h vs. 7.0 h,  $P=0.18$ ). Our study, based on a large multicenter sample of 2406 patients, revealed that children experiencing abdominal pain for more than 11.5 h

prior to visiting the emergency department had a heightened risk of RI following pneumatic reduction.

Mixed reports exist regarding the use of blood tests to predict short-term RI [10, 11]. This study collected blood test indexes from hospitalized children with acute intussusception and found that the number of white blood cells and hypersensitive C-reactive protein were independent predictors of reintussusception after pneumatic reduction. Delgado-Miguel et al. [21] also showed that C-reactive protein is an independent risk factor for intussusception surgical intervention. However, a retrospective study by Zhang et al. [22] involving 624 children found no correlation between C-reactive protein, leukocyte values, and the incidence of reintusions after enema, contradicting our findings. Further literature review revealed that Yang et al. [11] identified monocyte



**Fig. 3** 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



**Fig. 4** The nomogram for predicting the risk of recurrent in pediatric intussusception after pneumatic reduction

ratio as an independent risk factor for short-term RI, with children having a high monocyte ratio being more likely to experience early recurrence. Zhu et al. [23] discovered that peripheral blood monocyte chemotactic protein-1 (MCP-1) expression was elevated in children with short-term recurrence of primary intussusception, serving as a predictive risk factor for short-term recurrence. Overall, the reported results suggest a significant association between inflammatory factors and short-term RI, aligning with our own data analysis.

This retrospective study has certain limitations that need to be acknowledged. Firstly, there may be additional

risk factors, such as vomiting and environmental temperature, that were not considered in our analysis. Because this study was multicenter and the length data of some central intestinal invagination segments were missing, this index was not included in the analysis in this study. Secondly, the fasting time of children after pneumatic reduction could vary across the six medical institutions involved in the study, and its potential relationship with intussusception was not explored. Thirdly, partial data loss occurred due to some children's parents opting for automatic discharge after enema for various reasons. Moreover, the nomogram we have established has not



yet been validated with external data. Moving forward, future studies will address these limitations by aiming to develop a multi-modal prediction model with a larger sample size. The research team is conducting a prospective study of the risk factors for recurrent intussusception in more centers in hopes of creating an improved scoring system, and the results of the study will be published in a later paper.

## Conclusions

In this study, a nomogram was developed based on clinical risk factors to predict recurrent intussusception following pneumatic reduction in children. Age, abdominal pain time, white blood cell counts, and hypersensitive C-reactive protein levels were identified as predictors and incorporated into the nomogram. Internal validation demonstrated that this nomogram can offer a clear and convenient tool for identifying risk factors for recurrence of intussusception in children undergoing pneumatic reduction.

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We thank all the participants and researchers who participated in this study.

## Author contributions

All authors have approved the final version of the manuscript. JL, DZ and ZJ contributed equally to this paper. JL, HL and DZ designed the research, analyzed the data, and wrote the manuscript; XM, WX, and ZJ analyzed and interpreted the data; JL, HL and ZJ designed the research, analyzed the data, and corrected the manuscript. All authors contributed to the article and approved the submitted version.

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## Data availability

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

## Declarations

### 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. 2022 – 105), and all the legal guardians of children involved in this study signed the informed consent form.

### Consent for publication

Not applicable.

### Competing interests

The authors declare no competing interests.

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