

Original Article

Evaluating Preoperative Hematologic Markers in Differentiating Non-perforated and Perforated Appendicitis in Pediatric Asian Populations

Ying-Chiao Chou¹

Yu-Feng Tien¹

Li-Chin Cheng¹

Hsuan-Yi Huang¹

Tune-Yie Shin²

Chia-Lin Chou¹

¹Division of Colorectal Surgery, Department of Surgery, Chi-Mei Medical Center,

²Division of Pediatric Surgery, Department of Surgery, Chi-Mei Medical Center, Tainan, Taiwan

Key Words

Pediatric;

Perforated appendicitis;

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Purpose. Acute appendicitis is a common pediatric surgical emergency; however, its diagnosis remains challenging and appendicitis is frequently associated with a high rate of perforation, particularly among younger patients. With the goal of enhancing early detection and improving clinical outcomes, this study aimed to assess the utility of preoperative hematologic markers to distinguish between non-perforated and perforated appendicitis in Taiwanese pediatric patients.

Methods. This retrospective, single-center study conducted at Chi-Mei Hospital between 2019 and 2024 enrolled patients aged 18-years-old or younger diagnosed with acute appendicitis. Patients were categorized into perforated and non-perforated groups. Comprehensive clinical, laboratory, imaging, and operative data were systematically analyzed. Optimal hematologic marker cut-offs were determined using receiver operating characteristic (ROC) curve analysis and sensitivity and specificity were calculated.

Results. Of the 315 pediatric patients, 68 (21.59%) had histopathologically confirmed perforated appendicitis; these patients were younger, had longer hospital stays, and exhibited elevated neutrophil and platelet counts, monocyte-to-lymphocyte ratios (MLR), platelet-to-lymphocyte ratios (PLR), and C-reactive protein (CRP) levels (all $p < 0.05$). CRP (cut-off, 40.70 mg/L) had the highest diagnostic accuracy for perforation (area under the curve, 0.84; sensitivity, 84.21%; specificity, 76.63%).

Conclusions. CRP demonstrated the highest diagnostic accuracy for perforated appendicitis in pediatric patients. Although the PLR and MLR exhibited some diagnostic potential, their lower specificity limits their clinical utility. Further studies are required to establish the optimal CRP threshold for routine use.

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Acute appendicitis is the most common abdominal surgical emergency in pediatric patients, with a lifetime risk of approximately 7% in girls and 9% in boys.¹ Despite its high prevalence, the diagnosis and

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Correspondence to: Dr. Chia-Lin Chou, Division of Colorectal Surgery, Department of Surgery, Chi-Mei Medical Center, No. 901, Zhonghua Road, Yongkang Dist., Tainan 710, Taiwan. Tel: 886-6-281-2811; Fax: 886-6-281-4813; E-mail: clchou3@gmail.com & Dr. Tune-Yie Shin, Division of Pediatric Surgery, Department of Surgery, Chi-Mei Medical Center, No. 901, Zhonghua Road, Yongkang Dist., Tainan 710, Taiwan. Tel: 886-6-281-2811; Fax: 886-6-281-4813; E-mail: stone840728@yahoo.com.tw

management of appendicitis in children remain challenging. Perforated appendicitis is significantly more common among pediatric patients than in adults. The rate of perforation ranges from 20% to 74% in children, with some studies reporting nearly 100% perforation in infants under one year-of-age and rates of up to 69% in children under five-year-olds.²⁻⁴ In addition, studies have reported the odds of appendiceal rupture were 13% higher in African American children and 66% higher in Asian children compared to their white counterparts.⁵

The elevated risk of perforation in children can be attributed to several factors. First, children often present with a wide spectrum of atypical symptoms that are difficult to recognize. Second, young children's limited ability to effectively communicate their symptoms to their parents or healthcare providers frequently results in delayed diagnosis. Lastly, the relative absence of omental and intra-abdominal fat in younger children facilitates more rapid peritoneal dissemination of infection.^{6,7}

Therefore, early recognition and suspicion of perforation are critical, as timely diagnosis significantly influences clinical decision-making and the timing of surgical intervention. Prompt identification and management of appendicitis can reduce morbidity, shorten hospital stays, and lower healthcare costs. In recent years, increasing attention has been directed toward identifying reliable, accessible, and cost-effective methods for assessing the severity of appendicitis. Routine blood parameters have emerged as valuable adjuncts in this regard. Laboratory parameters associated with the severity of appendicitis include decreased serum sodium,^{4,9,10} elevated serum total bilirubin,^{4,8} erythrocyte sedimentation rate (ESR),¹¹ C-reactive protein (CRP),^{9,12,13} white cell count (WCC),^{10,12} neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), monocyte-to-lymphocyte ratio (MLR), and procalcitonin (PCT).¹⁴ However, the majority of these studies were conducted in American/White populations.

Given the differences in perforation rates between White and Asian children and the current lack of highly accurate validated biomarkers in Asian pediatric populations, this single-center study aimed to evaluate

the diagnostic utility of preoperative hematologic markers to distinguish between non-perforated and perforated appendicitis in Taiwanese children. Markers such as the WCC, NLR, MLR, PLR, and CRP were analyzed due to their routine availability, low cost, and relevance to systemic inflammatory responses. Improved identification of perforation risk may enhance early diagnosis and optimize clinical management for this vulnerable population of patients.

Materials and Methods

This retrospective, single-center study was conducted at Chi-Mei Hospital between January 2019 and December 2024. We included patients aged 18-years-old or younger who were diagnosed with acute appendicitis upon admission. Exclusion criteria included patients who had received antibiotic therapy prior to the diagnosis of appendicitis, in order to avoid potential interference with the accuracy of hematologic markers, and those with incomplete medical records. All remaining cases were deemed eligible for further analysis. Based on postoperative histopathological findings, patients were categorized into two groups: non-perforated appendicitis and perforated appendicitis.

Data were systematically collected using a standardized proforma, which included demographic characteristics, clinical symptoms, the findings of physical examinations, imaging results (including ultrasound and computed tomography), the duration of hospitalization, laboratory parameters (such as white cell count [WCC], neutrophil count, and C-reactive protein [CRP]), as well as the details of surgery including the surgical technique and histological outcomes.

Statistical analyses were performed using Statistical Package for the Social Sciences (SPSS), version 30.0 (SPSS Inc., Chicago, IL, USA). Categorical variables were compared using the chi-square test, and continuous variables were analyzed using Student's *t*-test. The diagnostic accuracy of hematologic markers for prediction of perforated appendicitis was assessed using receiver operating characteristic (ROC) curve

analysis to determine optimal cut-off values. Diagnostic performance was further evaluated by calculating the sensitivity, specificity, accuracy, positive predictive value (PPV), negative predictive value (NPV), positive likelihood ratio, and negative likelihood ratio. A p -value < 0.05 was considered statistically significant.

Results

A total of 365 pediatric patients diagnosed with acute appendicitis were initially considered for this study (Fig. 1). After applying the exclusion criteria, 37 patients were excluded due to receiving conservative (non-operative) treatment, 11 were excluded based on histopathological findings of a normal appendix, and two were excluded due to incomplete data. Ultimately, 315 patients were included in the final analysis. Of these, 247 patients were classified as having non-perforated appendicitis and 68 patients were classified as having perforated appendicitis based on post-operative histopathological examination. The demographic characteristics and clinical features of both groups are summarized in Table 1.

The mean age of the overall study population was 13.23 ± 3.84 years. Patients in the non-perforated group were significantly older (mean $\pm$ SD, 13.79 ± 3.68 years) compared to the patients in the perforated group (11.22 ± 3.75 years; $p < 0.001$). Males accounted for 66.98% of the cohort, and there was no significant difference in the sex distribution between the two groups ($p = 0.315$). The mean length of hospital stay (LOS) was 4.20 ± 2.52 days. The perforated appendicitis group had a significantly longer LOS (6.22 ± 4.40 days) compared to the non-perforated group (3.64 ± 1.18 days; $p < 0.001$).

The mean duration of symptoms was 1.71 ± 1.44 days. Patients in the perforated group exhibited a significantly longer duration of symptoms compared with those in the non-perforated group (2.75 ± 2.12 days vs. 1.44 ± 1.04 days, $p < 0.001$). The most common clinical symptoms included nausea or vomiting (52.06%), migratory pain (38.10%), and anorexia (20.63%). Anorexia was significantly more frequent in the perfo-

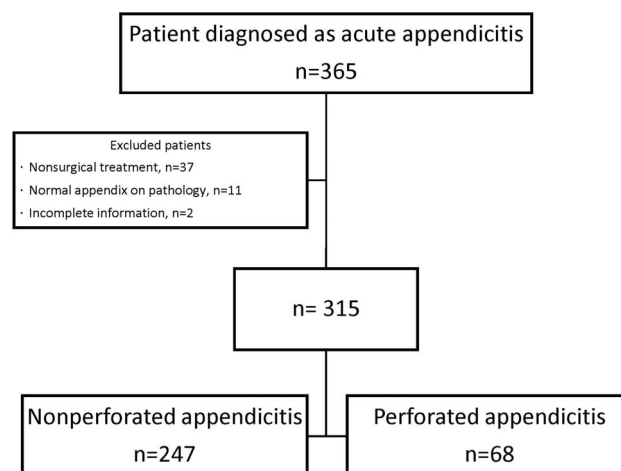


Fig. 1. Study flow chart outlining the selection process of pediatric patients diagnosed with acute appendicitis between January 2019 and December 2024.

rated group (29.41% vs. 18.22%; $p = 0.043$). The perforated group also demonstrated significantly higher rates of muscle guarding (41.18% vs. 6.48%; $p < 0.001$), rebound tenderness (51.47% vs. 25.51%; $p < 0.001$), and elevated body temperature (37.79 ± 1.08 °C vs. 37.15 ± 0.77 °C, $p < 0.001$).

All patients underwent imaging studies for suspected appendicitis. Contrast-enhanced abdominal computed tomography (CT) was most frequently employed (229/315, 72.70%). In addition, 25.71% of patients initially received abdominal ultrasound performed by a pediatric emergency physician. When ultrasound results were inconclusive or suggested perforation, an abdominal CT was subsequently performed. The radiologic criteria for diagnosing perforated appendicitis included the presence of extraluminal air, extraluminal appendicolith, an abscess, phlegmon, or a focal defect in the appendiceal wall.

The choice of surgical approach was at the discretion of the attending surgeon. Overall, 65.08% of patients underwent open appendectomy; 28.78% of these patients were diagnosed with perforated appendicitis, compared to 8.18% of patients who underwent laparoscopic appendectomy.

Comparative analysis of laboratory data revealed that the perforated group had significantly higher neutrophil counts ($13,411.20 \pm 5700.70$ vs. $12,073.79 \pm 4441.83$; $p = 0.04$) and platelet counts ($297,323.53 \pm 94,990.88$ vs. $271,619.43 \pm 70,313.71$; $p = 0.04$) than

Table 1. Demographic characteristics

	Nonperforated appendicitis (n = 247)	Perforated appendicitis (n = 68)	Overall appendicitis (n = 315)	p-value
Gender				0.315
Male	162 (65.59%)	49 (72.06%)	211 (66.98%)	
Female	85 (34.41%)	19 (27.94%)	104 (33.02%)	
Age (mean $\pm$ SD)	13.79 $\pm$ 3.68	11.22 $\pm$ 3.75	13.23 $\pm$ 3.84	< 0.001
Symptom				
Duration (day)	1.44 $\pm$ 1.04	2.75 $\pm$ 2.12	1.71 $\pm$ 1.44	< 0.001
Nausea or vomiting	126 (51.01%)	38 (55.88%)	164 (52.06%)	0.477
Anorexia	45 (18.22%)	20 (29.41%)	65 (20.63%)	0.043
Migratory pain	93 (37.65%)	27 (39.71%)	120 (38.10%)	0.757
Physical examination				
RLQ tenderness	241 (97.57%)	48 (70.59%)	289 (91.75%)	< 0.001
Muscle guarding	16 (6.48%)	28 (41.18%)	44 (13.97%)	< 0.001
Rebound pain	63 (25.51%)	35 (51.47%)	98 (31.11%)	< 0.001
Temperature	37.15 $\pm$ 0.77	37.79 $\pm$ 1.08	37.29 $\pm$ 0.89	< 0.001
Image finding				< 0.001
Non-perforated	236 (95.55%)	42 (61.76%)	278 (88.25%)	
Perforated	9 (3.64%)	26 (38.24%)	35 (11.11%)	
Surgical procedure				< 0.001
Open	146 (59.11%)	59 (86.76%)	205 (65.08%)	
Laparoscopy	101 (40.89%)	9 (13.24%)	110 (34.92%)	
Length of stay (day) (mean $\pm$ SD)	3.64 $\pm$ 1.18	6.22 $\pm$ 4.40	4.2 $\pm$ 2.52	< 0.001
Pre-operative waiting time (day) (mean $\pm$ SD)	0.31 $\pm$ 0.50	0.25 $\pm$ 0.44	0.3 $\pm$ 0.48	0.0385
Lab data				
White cell count	14678.22 $\pm$ 4458.77	15820.59 $\pm$ 5915.24	14924.83 $\pm$ 4823.17	0.084
Neutrophil count	12073.79 $\pm$ 4441.83	13411.20 $\pm$ 5700.70	12362.50 $\pm$ 4763.95	0.04
Monocyte count	712.81 $\pm$ 427.95	788.89 $\pm$ 455.39	729.23 $\pm$ 434.41	0.201
Lymphocyte count	1747.11 $\pm$ 882.79	1493.01 $\pm$ 806.94	1682.25 $\pm$ 872.04	0.033
Platelet count	271619.43 $\pm$ 70313.71	297323.53 $\pm$ 94990.88	277168.25 $\pm$ 76882.24	0.04
NLR	9.66 $\pm$ 8.23	11.85 $\pm$ 5.55	10.13 $\pm$ 8.33	0.055
MLR	0.52 $\pm$ 0.44	0.67 $\pm$ 0.55	0.55 $\pm$ 0.47	0.021
PLR	199.26 $\pm$ 118.73	255.26 $\pm$ 162.27	211.35 $\pm$ 131.13	0.009
CRP (mg/L)	36.68 $\pm$ 61.22	126.95 $\pm$ 95.66	58.03 $\pm$ 79.89	< 0.001

RLQ: right lower quarter; NLR: neutrophil-to-lymphocyte ratio; MLR: monocyte-lymphocyte ratio; PLR: platelet-to-lymphocyte ratio; CRP: C-reactive protein.

the non-perforated group. Conversely, the perforated group had significantly lower lymphocyte counts (1,493.01 $\pm$ 806.94 vs. 1,747.11 $\pm$ 882.70; $p = 0.033$). Inflammatory ratios, including the monocyte-to-lymphocyte ratio (MLR) and platelet-to-lymphocyte ratio (PLR), were also significantly elevated in the perforated group (MLR: 0.67 $\pm$ 0.55 vs. 0.52 $\pm$ 0.44, $p = 0.021$; PLR: 255.26 $\pm$ 162.27 vs. 199.26 $\pm$ 118.73, $p = 0.009$). In addition, CRP was markedly elevated in the perforated group (126.95 $\pm$ 95.66 mg/L vs. 36.68 $\pm$ 61.22 mg/L; $p < 0.001$).

Receiver operating characteristic (ROC) curve

analyses were performed to evaluate the diagnostic performance of various inflammatory markers to differentiate between perforated and non-perforated appendicitis (Table 2, Fig. 2). Among the markers analyzed, CRP exhibited the highest diagnostic accuracy, with an area under the curve (AUC) of 0.84 (95% CI: 0.79-0.90), sensitivity of 84.21%, and specificity of 76.63% based on an optimal cut-off value of 40.70 mg/L. The positive predictive value (PPV) and negative predictive value (NPV) were 52.08% and 94.12%, respectively. The positive likelihood ratio (PLR) and negative likelihood ratio (NLR) were 3.50 and 0.21,

Table 2. Receiver operating characteristic analysis of inflammatory markers

	AUC (95% CI)	Cutoff value	Sensitivity	Specificity	PPV	NPV	Positive likelihood ratio	Negative likelihood ratio	p-value
NLR	0.59 (0.50-0.67)	6.96	70.18%	47.28%	29.32%	83.33%	1.33	0.65	0.039
MLR	0.58 (0.49-0.67)	0.51	54.39%	65.76%	32.98%	82.31%	1.59	0.69	0.045
PLR	0.61 (0.53-0.70)	184.70	63.16%	56.52%	31.03%	83.20%	1.45	0.65	0.042
CRP (mg/L)	0.84 (0.79-0.90)	40.70	84.21%	76.63%	52.08%	94.12%	3.50	0.21	< 0.001

NLR: neutrophil-to-lymphocyte ratio; MLR: monocyte-lymphocyte ratio; PLR: platelet-to-lymphocyte ratio; CRP: C-reactive protein; AUC: area under curve; PPV: positive predictive value; NPV: negative predictive value.

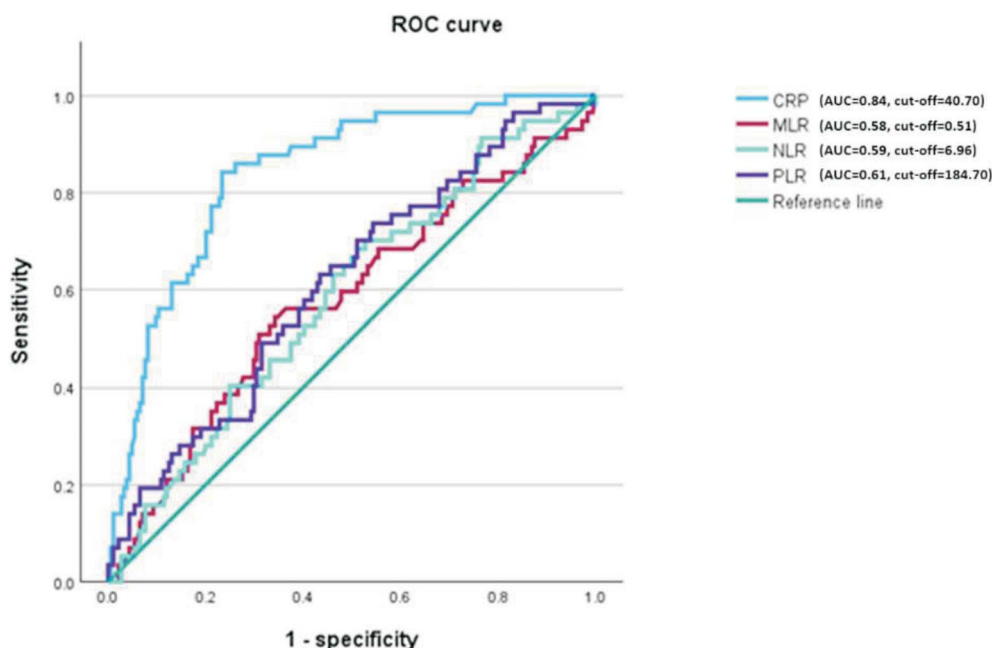


Fig. 2. Receiver operating characteristic (ROC) curves illustrating the diagnostic accuracy of C-reactive protein (CRP), neutrophil-to-lymphocyte ratio (NLR), monocyte-lymphocyte ratio (MLR), platelet-to-lymphocyte ratio (PLR) in differentiating perforated from non-perforated appendicitis among pediatric patients.

respectively, which indicates that CRP may serve as a highly reliable biomarker for the early detection and exclusion of perforated appendicitis in pediatric patients.

The optimal cut-off for the neutrophil-to-lymphocyte ratio (NLR) was 6.96, which yielded an AUC of 0.59 (95% CI: 0.50-0.67, $p = 0.039$), sensitivity of 70.18%, specificity of 47.28%, positive predictive value (PPV) of 29.32%, and negative predictive value (NPV) of 83.33%. Based on the optimal cut-off of 0.51, the MLR had an AUC of 0.58 (95% CI: 0.49-0.67, $p = 0.045$), sensitivity of 54.39%, specificity of 65.76%, PPV of 32.98%, and NPV of 82.31%. Based on the optimal cut-off of 184.70, the PLR had an AUC

of 0.61 (95% CI: 0.53-0.70, $p = 0.042$), with a sensitivity of 63.16%, specificity of 56.52%, PPV of 31.03%, and NPV of 83.20%.

Discussion

Multiple risk factors have been identified for perforated appendicitis in children, including younger age at presentation, a longer duration of symptoms, and non-specific manifestations such as anorexia and emesis.^{4,15} Our analysis supports these observations, as we observed significant differences in several clinical and laboratory characteristics between the perfo-

rated and non-perforated groups. Patients with perforated appendicitis were significantly younger ($p < 0.001$) and exhibited a higher prevalence of anorexia ($p = 0.043$). Moreover, patients with perforated appendicitis exhibited more pronounced peritoneal signs, including muscle guarding and rebound tenderness, which are suggestive of advanced disease progression.

In this study, imaging showed an overall accuracy of 83.70%, with a sensitivity of only 38.24% for detecting perforated appendicitis, but a high specificity of 96.33%. CT demonstrated an accuracy of 86.42%, with a sensitivity of 53.19% and a high specificity of 95.05%. Ultrasonography (echo) had an accuracy of 76.54%, with a very low sensitivity of 5.00%, but a specificity of 100.0%. CT demonstrated a false-negative rate of 11.28%, compared with 23.75% for ultrasonography. Approximately 15.11% of patients with initially non-perforated imaging findings were later confirmed to have perforation; however, this may have been attributable either to limitations in imaging accuracy or to disease progression in the period between imaging and surgery — despite an average time to surgery of less than 12 hours. These findings highlight the limitations of relying solely on imaging modalities and emphasize the importance of assessing the correlations between clinical and laboratory findings. Elinet et al. identified radiologic features such as the presence of an abscess, intraluminal appendicolith, and loss of the echogenic submucosal layer of the appendiceal wall as indicators of perforation.¹⁶ Similarly, Horrow et al. reported that the presence of focal defects in the appendiceal wall on CT only had a sensitivity of 64% for perforation.¹⁷ Additionally, the operator-dependency of ultrasound and concerns regarding radiation exposure from CT imaging in children must be considered.

We also observed a higher rate of perforation among patients who underwent open appendectomy compared to the group that received laparoscopic surgery. This difference may reflect the surgeons' preference, as the only pediatric surgeon at our center performs open appendectomy in nearly all cases. Younger patients are more frequently admitted under pediatric surgical care and are therefore more likely to undergo open surgery, whereas older children might be

admitted to the hospital under the care of a general surgeon when the only pediatric surgeon was unavailable on duty at that time. Among 121 children admitted to the general surgical service, the majority underwent laparoscopic appendectomy, while 11 (9.09%) underwent open appendectomy. Of these, seven had preoperative CT findings suggestive of acute appendicitis, which was confirmed on pathology, while four had preoperative CT findings suspicious for perforation accompanied by peritonitis. In addition, the duration of hospital stay was longer for the perforated group, which reflects the higher clinical and economic burden associated with perforation and reinforces the need for early and accurate identification to optimize treatment strategies, improve patient outcomes, and reduce healthcare costs.

We also investigated the predictive value of several inflammatory markers to identify perforated appendicitis. Previous studies have established CRP as a reliable marker. Duman et al. reported CRP resulted in an AUC of 0.897, which indicates strong discriminatory capability.¹⁸ Similarly, Lobo et al. identified a CRP level of > 4.3 mg/dL achieved 74% sensitivity and 77% specificity to diagnose complicated appendicitis.¹⁹ Furthermore, Buyukbesse demonstrated that combining a WBC $\geq 13,100/\mu\text{L}$ and CRP level of ≥ 1.17 mg/dL yielded a sensitivity of 98.7% and NPV of 99.5% for perforation, with CRP alone achieving an AUC of 0.887.²⁰

The neutrophil-to-lymphocyte ratio (NLR) has been reported to exhibit varied predictive value for perforation, with cutoffs ranging from 6.59 to 10.4 leading to AUC values above 0.7 in several studies.^{18,21-24} PLR has also emerged as a potential predictor. Çelik et al. reported a PLR cutoff of 284 had an AUC of 0.647 for complicated appendicitis,²³ while Julio et al. found PLR (cut-off, 213.3) to be the most accurate predictor, with an AUC of 0.802, sensitivity of 60%, and specificity of 85%.²² In addition, Pehlivanli and Aydin identified a PLR cutoff of 193.67 resulted in an AUC of 0.694.²⁵

However, most of these studies were conducted outside of Asia; thus, there is a need for region-specific validation. A retrospective study in China found that CRP, the pediatric appendicitis score (PAS), and

the diameter of the appendix were independent risk factors for complicated appendicitis in children under 3-years-old, with CRP (cut-off, 50.22 mg/L) resulting in an AUC of 0.766.²⁶ Similarly, a Taiwanese review confirmed the utility of CRP in distinguishing complicated from uncomplicated appendicitis in children, identifying an optimal CRP cut-off value of 4.06 mg/dL, which yielded a remarkable AUC of 0.928.²⁷ In light of the findings from the Taiwanese study and our own results, it appears that, in pediatric appendicitis within the Taiwanese population, a CRP level above 4 mg/dL may serve as a potential indicator of perforation.

Our findings are consistent with these prior reports. Among the biomarkers we evaluated, CRP demonstrated the highest diagnostic accuracy for perforation, with superior sensitivity, specificity, and predictive values. In addition, the PLR was significantly higher in the perforated group; however, its diagnostic performance was moderate (AUC = 0.61; sensitivity = 63.16%; specificity = 56.52%); thus, the PLR has limited standalone clinical utility. Likewise, the MLR (AUC = 0.58) and NLR (AUC = 0.59) exhibited only modest diagnostic performance. While these markers may aid in risk stratification, their limited accuracy indicates the need for development of a multi-parameter approach.

Several limitations of this study should be noted. First, the retrospective design introduces potential selection bias and dependence on the accuracy of recorded data. Second, the study cohort was limited to a single institution and specific age group, which potentially affects the generalizability of our findings. Third, although CRP demonstrated high diagnostic value, the lack of standardized thresholds may limit its clinical applicability. In addition, potential variability in marker levels due to comorbidities, medications, or immune responses may also confound interpretation of our results, and these issues could not be fully accounted for in this analysis.

Conclusions

Although several inflammatory markers demon-

strated potential to predict perforated appendicitis, CRP exhibited the highest sensitivity, specificity, and overall diagnostic accuracy, and may hold value as a reliable biomarker for identifying perforation in pediatric patients. While the platelet-to-lymphocyte ratio (PLR) showed moderate diagnostic performance, its lower specificity limits its standalone clinical utility. Overall, our findings suggest that CRP may serve as a valuable predictive marker for perforated appendicitis in pediatric patients. However, future studies involving larger, multi-center cohorts and the inclusion of additional inflammatory markers are warranted to develop more comprehensive and robust diagnostic models.

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原 著

術前血液學指標在區分亞洲兒童非穿孔與穿孔性闌尾炎之應用評估

周瑛喬¹ 田宇峯¹ 鄭立勤¹ 黃亘毅¹ 石敦義² 周家麟¹¹永康奇美醫療財團法人奇美醫院 外科部 大腸直腸外科²永康奇美醫療財團法人奇美醫院 外科部 小兒外科

目的 急性闌尾炎是常見的兒童外科急症，但其診斷仍具挑戰性，特別是在年幼兒童中，常導致較高的穿孔率。為了提升早期診斷與臨床預後，本研究旨在評估術前血液學指標在區分台灣兒童非穿孔性與穿孔性闌尾炎的應用價值。

方法 本回溯性單一中心研究於 2019 年至 2024 年間在奇美醫院進行，納入 18 歲以下的急性闌尾炎之病患。依病理結果分為穿孔組與非穿孔組。系統性分析臨床、實驗室、影像學及手術資料，並透過接受者操作特徵曲線分析血液學指標的臨界值，計算其靈敏度與特異性。

結果 在 315 位患者，其中 68 例 (21.59%) 經組織病理學確認為穿孔性闌尾炎。這些患者年齡顯著較小，住院天數較長，且具有較高的嗜中性球數、血小板數、單核球與淋巴球比值、血小板與淋巴球比值，以及 C 反應蛋白濃度 ($p < 0.05$)。其中，C 反應蛋白在診斷穿孔性闌尾炎方面表現最佳 (曲線下面積 = 0.84；敏感性：84.21%；特異性：76.63%)，最佳臨界值為 40.70 mg/L。

結論 C 反應蛋白對於識別兒童穿孔性闌尾炎具最高的診斷準確性。雖然血小板與淋巴球比值、單核球與淋巴球比值也具一定診斷價值，但因其特異性較低，臨床應用仍有限。未來仍需進一步研究，以確立適用於臨床的 C 反應蛋白最佳臨界值。

關鍵詞 兒童、穿孔性闌尾炎、C 反應蛋白。