

The Significance of Combined Detection of Ultrasonography, Pediatric Appendicitis Score and C-reactive Protein in the Diagnosis and Pathological type of Acute Appendicitis in Children

Hai Hu

The First Affiliated Hospital of Guangxi Medical University

Minghui Lin

The First Affiliated Hospital of Guangxi Medical University

Wei Li

The First Affiliated Hospital of Guangxi Medical University

Jiabo Chen

The First Affiliated Hospital of Guangxi Medical University

Cheng Su

The First Affiliated Hospital of Guangxi Medical University

Jinhong Li

The First Affiliated Hospital of Guangxi Medical University

Jianyuan Huang

The First Affiliated Hospital of Guangxi Medical University

Yige Lou (✉ lyg6829@163.com)

The First Affiliated Hospital of Guangxi Medical University

Research Article

Keywords: acute appendicitis, children, ultrasonography, Pediatric Appendicitis Score, C-reactive protein, histopathology

Posted Date: November 2nd, 2023

DOI: <https://doi.org/10.21203/rs.3.rs-3522270/v1>

License: © ⓘ This work is licensed under a Creative Commons Attribution 4.0 International License. [Read Full License](#)

Additional Declarations: No competing interests reported.

Abstract

Background: As one of the most common diseases of acute abdomen, early diagnosis of acute appendicitis remains a vital issue. This study aims to explore the value of combined ultrasonography, Pediatric Appendicitis Score and C-reactive protein in the diagnosis and pathological types of appendicitis in children.

Method: A total of 268 children with acute abdominal pain admitted to our center between January 2017 and January 2020 were retrospectively analyzed and divided into group acute appendicitis and group non-acute appendicitis based on the surgical findings and pathological findings. Group acute appendicitis was further divided into three groups based on the types of pathology, group simple appendicitis, group suppurative appendicitis and group gangrenous appendicitis.

Results: Pediatric Appendicitis Score and level of C-reactive protein in group acute appendicitis were higher than group non-acute appendicitis ($P < 0.05$). The areas under the receiver operating characteristic curve of Pediatric Appendicitis Score, C-reactive protein and ultrasonography for acute appendicitis were 0.871, 0.777 and 0.897, respectively ($P < 0.001$). The sensitivity and negative predictive value of ultrasonography combined with Pediatric Appendicitis Score and C-reactive protein in diagnosing acute appendicitis were higher than ultrasonography and CRP, while the specificity and positive predictive value were lower ($P < 0.05$). The C-reactive protein in the acute complicated appendicitis was significantly higher than simple appendicitis, and the areas under the ROC curve of C-reactive protein and ultrasonography in diagnosing acute complicated appendicitis were 0.814(0.762-0.867) and 0.861(0.812-0.909). The sensitivity of ultrasonography combined with C-reactive protein in diagnosing acute complicated appendicitis was 98.21%, which was significantly higher than that of ultrasonography and CRP alone ($P < 0.05$). The sensitivities of ultrasonography for different pathological types of appendicitis were 78.95% for acute simple appendicitis, 81.97% for acute suppurative appendicitis and 92.16% for acute gangrenous appendicitis. The diagnostic results of ultrasonography for different pathological types of appendicitis in children were consistent with those of pathological examination (Kappa=0.888; $P < 0.001$).

Conclusion: The combination of ultrasonography, Pediatric Appendicitis Score and C-reactive protein detection is helpful to the accurate diagnosis of acute appendicitis, and ultrasonography combined with CRP may contribute to diagnosing pathological type of appendicitis in children, providing important evidence for clinical diagnosis.

INTRODUCTION

Acute appendicitis was one of the most common acute abdominal diseases in pediatric surgery, 1–8% of which diagnosed with acute appendicitis [1]. The onset peaks age of acute appendicitis in children are 10 and 19 years old, respectively [2]. Acute appendicitis was divided into acute simple appendicitis and acute complicated appendicitis according to intraoperative findings and postoperative pathological report. Acute simple appendicitis was defined as inflammation of the appendix but without gangrene, perforation, purulent liquid in the abdominal cavity and so on. In contrast, acute complicated appendicitis includes appendiceal gangrene, periappendiceal abscess, and effusion, combined with or without appendiceal perforation [3]. For acute simple appendicitis (except with calculus), conservative treatment with antibiotics is considerable, while acute complicated appendicitis requires surgical treatment [4]. Perforation is the most concerning complication of acute appendicitis, which may lead to abscesses, peritonitis, bowel obstruction, fertility issues, and sepsis [5]. Research showed the rate of missed diagnosis for children under 3 years old was fairly high (70%-100%), and 19%-57% for preschool children, which declined to 12–28% for school-age children [6]. Consequently, the early diagnosis and assessment of pathological types of acute appendicitis are of great significance for making decisions for treatment.

Pediatric Appendicitis Score (PAS) is a scoring system developed in a prospective cohort study of 1170 patients by Madan Samuel in 2002 and contains 8 variables that are statistically significant for acute appendicitis [7]. Derived from visceral adipose tissue during acute inflammation, the expression of C-reactive protein (CRP) related to severity of inflammation [8]. Studies showed that $CRP \geq 10\text{mg/L}$ could be a strong predictor of acute appendicitis in children under 6 years of age [9]. Imaging examinations also play prominent roles in the diagnosis of acute appendicitis. Characterized by simplicity, economy, free of ionization radiation, high sensitivity and specificity for the diagnosis of acute appendicitis, and value for distinguish different pathological types, ultrasonography (US) was widely used in children with suspected appendicitis in spite of many distractions like obesity, intestinal gas [10, 11]. Guidelines for the management and treatment of acute appendicitis discussed and developed by the World Society of Emergency Surgery (WSES) in 2015, updated again in July 2019, suggested that combining US with clinical scoring may significantly improve diagnostic sensitivity and specificity [4, 12]. However, there were rarely studies combined clinical scores, inflammatory markers, and imaging to diagnose acute appendicitis in children. Ultrasonography combined Pediatric Appendicitis Score and CRP might be a solution to the early diagnosis of acute appendicitis in pediatric, all of which have been proved to be strongly related to acute appendicitis, and may be instrumental in the clinical diagnosis of the type of acute appendicitis. In this study, clinical data of 268 children with suspected acute appendicitis were retrospectively reviewed to assess the roles of US, PAS and CRP in the early diagnosis of acute appendicitis.

INFORMATION AND METHODS

Subjects

A total of 268 patients suffering acute abdominal pain, visited Department of Pediatric Surgery and the Pediatric Surgery Clinic of The First Affiliated Hospital of Guangxi Medical University between 2017 and 2020, were retrospectively analyzed. The patients, 154 males and 114 females, ranging from 2 to 14 years old (6.88 years old \pm 1.98 years old, 154 males and 114 females), were divided into group non-acute appendicitis (NAA) and group acute appendicitis (AA), where group AA was further divided into group A (38 cases of simple appendicitis), group B (61 cases of suppurative appendicitis) and group C (51 cases of gangrenous appendicitis). Studies involving human participants were reviewed and approved by the ethics committee of The First Affiliated Hospital of Guangxi Medical University. And the exclusion criteria were: (1) children > the age of 16; (2) final diagnosis of chronic appendicitis; (3) abdominal pain caused by abdominal trauma or surgery; (4) children with incomplete clinical data.

Methods

For patients admitted to our center, blood routine examination, CRP and US were performed immediately after the consent of the patients or their families. Blood routine examination was measured by Beckman-Coulter LH750 Automatic Blood Cell Counter, CRP by rate turbidimetric assay with Beckman ARRAY360 specific protein analyzer, both of which were performed by the Laboratory Department of our center.

All ultrasonic inspection reports were offered by the Department of Ultrasound in our center. PHILIPS EPIQ5 color Doppler ultrasound diagnostic instrument was used for suspecting acute appendicitis, with the low frequency probe frequency of 5.0 MHz, and the high frequency probe frequency of 10.0 ~ 14.0 MHz. From the hepatic inferior margin to the pelvis, multiple sections of the abdomen were examined by ultrasound probes, particularly focusing on pressure points with patients in the supine position. For the older children with a thick abdominal wall, low-frequency probe was first used for detecting suspicious areas, where high-frequency ultrasound probe was switched for further investigation and confirmation. The contents of observation included the position of appendix, shape, maximum diameter, structure and continuity of the appendiceal wall, lumen echo, the surrounding tissues, effusion around the appendix, adhesion with surrounding organs, and mass around the appendix. The clearest images were retained and then the ultrasonic features recorded.

The PAS was applied to assist in diagnosing appendicitis, including migration of pain (score-1), anorexia (score-1), nausea or vomiting (score-1), tenderness in the right lower quadrant of the abdomen (score-2), pain with cough/hopping/percussion (score-2), elevated temperature (score-1), leukocytosis (score-1), and Differential WBC count with a left shift (score-1). The higher the PAS of patients, the higher the risk of acute appendicitis [13]. In this study, PAS was evaluated by two patient and experienced pediatric surgeons, and the third surgeons would intervene in the evaluation till consensus reached when necessary.

Statistical Methods

Data was analyzed by the statistical software SPSS 24.0 and a $P < 0.05$ was considered statistically significant. Normally distributed continuous variables were expressed as mean \pm standard deviation ($\bar{x} \pm SD$), and non-normally distributed continuous variables were expressed as the median (interquartile range). Categorical variables were expressed as percentages (%). Normality of data was evaluated by Shapiro-Wilk test and normal distribution were found ($P < 0.001$). Continuous variables were compared between groups using the t-test, and categorical variables were compared by the chi-squared test. The receiver operating characteristic (ROC) curve was used to evaluate the diagnostic efficacy of these examinations in various types of appendicitis in children. Kappa test was used to assess the consistency of ultrasonic diagnosis and pathological examination in children with different pathological types of appendicitis.

RESULTS

General Data

The definitive diagnoses of 268 patients were listed in Table 1. Among the 268 patients, a total of 150 patients with diagnosis of acute appendicitis were incorporated into the group AA, while the others in group NAA, and the general data of the two groups were compared (see Table 2). No significant difference in age, gender, height and weight between these two groups was found ($P > 0.05$).

Table 1
Final diagnosis for the 268 patients

Final diagnosis	No.
Simple appendicitis	38
suppurative appendicitis	61
Gangrenous appendicitis	51
Lymphadenitis	28
Omental torsion	17
Diverticulitis, enteritis	15
Gynecologic conditions	21
Urinary infection	25
Other surgical condition	12
Total	268

Table 2
Comparison of general date, PAS and CRP between the group NAP and group AP

General date	NAA(N = 150)	AA(N = 118)	t or χ^2 - value	P- value
Gender(male,%)	58.00	56.78	0.400	0.841
Age(Mean \pm SD, year)	6.97 \pm 2.04	6.81 \pm 1.94	0.0626	0.532
Weight(Mean \pm SD, kg)	27.53 \pm 7.69	26.87 \pm 7.47	0.713	0.476
Height(Mean \pm SD, cm)	118.90 \pm 13.41	118.11 \pm 12.99	0.610	0.629
PAS (Mean \pm SD)	4.64 \pm 1.33	7.22 \pm 1.69	9.269	< 0.001*
CRP(Mean \pm SD, mg/L)	26.24 \pm 11.50	35.71 \pm 9.46	3.073	< 0.001*
CRP, C-reactive protein; PAS, Pediatric appendicitis score;				
NAA, group non-acute appendicitis; AA, group acute appendicitis				
* means P-value < 0.05				

Analysis of Diagnostic Methods

PAS, CRP and US in Acute Appendicitis

between group AA and group NAA, PAS and CRP in group AA were significantly higher than Group NAA ($P < 0.05$, see Table 2). To further explore the diagnostic value, ROC curve of US, PAS and CRP for diagnosing acute appendicitis was drawn (see Fig. 1). The areas under the ROC curve (confidence interval 95%) of US, PAS and CRP were 0.897(0.857–0.937), 0.871 (0.829–0.912) and 0.777 (0.716–0.838), respectively ($P < 0.05$), and the cutoff value of PAS and CRP were 6 and 27.06 mg/L, determined by the maximum value of Youden index. And the diagnostic value of these methods was researched (see Table 3). Among the three groups of comparison between PAS, CRP and US, the diagnostic value of US is the best, with the largest area under the ROC curve and the largest Yoden index.

Table 3
Value of modified PAS, CRP and ultrasonography in the diagnosis of acute appendicitis

Diagnostic methods	Sensitivity(%)	Specificity (%)	Positive predictive value(%)	Negative predictive value(%)	Positive likelihood ratio	Negative likelihood ratio	Youden index
PAS (≥ 6) ^a	82.67 (124/150)	89.83 (106/118)	91.18 (124/136)	80.30 (106/132)	8.129	0.193	0.725
CRP (≥ 27.06 mg/L) ^a	86.00 (129/150)	71.19 (84/118)	79.14 (129/163)	80.00(84/105)	0.985	0.197	0.572
Ultrasonography	88.39 (137/150)	88.50 (100/118)	91.33 (137/155)	84.75 (100/113)	7.683	0.131	0.769

^a means the cutoff value of PAS and CRP in judging acute appendicitis was 5.5 and 27.06 mg/L, respectively

Combined with Three methods to Diagnose Appendicitis

The sensitivity and negative predictive value of combination of US, PAS and CRP in the diagnosis of acute appendicitis was 99.33% and 98.46%, which was significantly higher than US alone ($P < 0.05$), though the specificity of combination of US, PAS and CRP was lower ($P < 0.05$). The positive predictive value of the combination of US, PAS and CRP were 73.40%, lower than US alone ($P > 0.05$; see Table 4).

Table 4
Value of combination of ultrasonography, PAS and CRP in the diagnosis of acute appendicitis

Diagnostic methods	Sensitivity(%)	Specificity (%)	Positive predictive value(%)	Negative predictive value(%)	Youden index
Ultrasonography alone	88.39 (137/150)	88.50 (100/118)	91.33 (137/155)	84.75 (100/113)	0.769
Combination of ultrasonography, PAS and CRP	99.33 (149/150)	54.24 (64/118)	73.40 (149/203)	98.46(64/65)	0.536
χ - value	10.789	29.804	12.289	5.656	
P -value	0.001*	< 0.001*	< 0.001*	0.017*	
* means P -value < 0.05					

CRP and US for Diagnosing Acute Complicated Appendicitis

The ROC curve of CRP and US for diagnosing acute complicated appendicitis was drawn (see Fig. 2), the AUC of which were 0.777(0.716–0.838) and 0.897(0.857–0.937) with $P < 0.05$. We have also found that US is excellent at ruling out acute complicated appendicitis, with the sensitivity of 86.60%. For acute complicated appendicitis, the sensitivity and negative predictive value of the combination of US and CRP were 98.21% and 98.37%, which were higher than US alone ($P < 0.05$; see Table 5).

Table 5
Value of combination of ultrasonography and CRP in the diagnosis of acute complicated appendicitis

Diagnostic methods	Sensitivity(%)	Specificity (%)	Positive predictive value (%)	Negative predictive value(%)	Youden index
Ultrasonography alone	75.00 (84/112)	91.67 (143/156)	86.60 (84/97)	83.63 (143/171)	0.667
Combination of ultrasonography and CRP	98.21 (110/112)	77.56 (121/156)	75.86 (110/146)	98.37 (121/123)	0.862
χ - value	10.539	1.927	0.004*	6.082	
P -value	0.001*	0.165	0.950	0.014*	
* means P -value < 0.05					

Analysis of Different Types of Acute Appendicitis

Among the three groups of acute appendicitis, there was no significant difference of PAS ($P > 0.05$), while CRP of children with acute complicated appendicitis was significantly higher than that of simple appendicitis ($P < 0.05$; see Table 6). The diagnostic accuracies of US for pathological types of appendicitis were 78.95% for acute simple appendicitis, 81.97% for acute suppurative appendicitis and 92.16% for acute gangrenous appendicitis. And the Kappa value of 0.888 ($P < 0.05$) indicates the consistency of US and pathological examination in children with different pathological types of appendicitis was excellent (see Table 7). The ultrasound manifestations of the normal appendix and various types of appendicitis are as follows (see Table 8).

Table 6
Comparison of PAS and CRP in patients with acute appendicitis

Groups	No.	PAS(Mean ± SD)	CRP(Mean ± SD, mg/L)
A	38	6.95 ± 1.64	31.03 ± 9.65
B	61	7.28 ± 1.52	37.06 ± 8.15 ^a
C	51	7.47 ± 1.67	38.83 ± 7.38 ^a
χ ² -value		2.240	10.23
P-value		0.110	< 0.001*
A, group simple appendicitis			
B, group suppurative appendicitis			
C, group gangrenous appendicitis			
^a means compare with group A, P < 0.05			
* means P-value < 0.05			

Table 7
Comparison of ultrasonographic and pathological diagnosis of appendicitis in children (No.)

Pathological diagnosis	Ultrasonographic diagnosis		
	Simple appendicitis	Suppurative appendicitis	Gangrenous appendicitis
Simple appendicitis	30	2	0
Suppurative appendicitis	2	50	2
Gangrenous appendicitis	0	4	47
Consistency between ultrasonic and pathological examination: kappa = 0.888, P-value < 0.001.			

Table 8
Ultrasonic features of appendices

Classification of appendicitis	Diameter	Appendiceal wall	Lumen of the appendix
Normal appendix	Usually less than 6 mm	Clearly layered, no thicker than 2 mm	With or without small amount of fluid
Simple appendicitis	Diameter ≥ 6mm	Clear hierarchical boundaries	Small amount of fluid in the cavity
Suppurative appendicitis	Swollen, with the rough and fuzzy outline	"Target ring" sign transversely, "bilateral" sign lengthwise	Echoes of stercolith could be found

DISCUSSION

The appendix cavity is blocked by bezoar or food debris as the narrow inner diameter of the appendix and the easily twisted appendix in children. And once bacteria invade the appendix wall, the inflammation of the appendix appears. Different from adult patients, accurate diagnosis in children probably remain difficult due to atypical symptoms, uncooperative physical examination and changes in patients' conditions.

As the two most popular clinical scoring systems for use in children, the Alvarado score and PAS are widely studied and appreciated in excluding acute appendicitis [4]. And the American College of Emergency Physicians approved that application of the Alvarado score as a triage clinical prediction rules that can be applied to 'rule out' appendicitis at a score below 5 points (sensitivity 94–99%) [14], while PAS has successfully detected cases of appendicitis due to its high diagnostic sensitivity[7]. In this study, with the cutoff value of 6, the sensitivity and specificity of PAS in the diagnosis of acute appendicitis were 82.67% (124/150) and 89.83% (106/118), respectively. When PAS not less than 5, the sensitivity and specificity were 93.33% (140/150) and 60.17% (71/118). The sensitivity and specificity are not satisfactory roughly because some preschool children had atypical clinical symptoms, uncooperative physical examination and changes in patients' conditions quickly, which is similar to Song's study[15]. However, PAS has no significant difference in the pathological types of acute appendicitis, and further diagnosis may need to be combined with other serum markers and imaging examinations.

As for the diagnostic efficiency of CRP in acute complicated appendicitis, the cutoff value of CRP in this study was 32.26mg/mL, the sensitivity was 79.46% (89/112), and the specificity was 79.49% (124/156). It has been reported that CRP level is correlated with the severity of appendicitis [16], which is consistent with our results. However, even if CRP at normal levels, that doesn't rule out the possibility of acute appendicitis. And the diagnosis of appendicitis should be combined with clinical judgment and inflammatory markers [17]. Laboratory markers that may be helpful in the diagnosis of pediatric acute appendicitis are being widely investigated currently, where some marker roles are certain and some remain to be seen. For instance, pentraxin3 levels are helpful in diagnosing acute appendicitis [18], while red cell distribution width remains debatable [19].

US plays an important part in the diagnosis and pathological classification of acute appendicitis. The use of clinical decision rules in conjunction with ultrasonography reduces the use of computed tomography (CT) in the evaluation of suspected appendicitis [5]. With the gradual understanding of ultrasound features of patients with appendicitis, US has almost as high diagnostic value as CT, a backup option, which is radioactive and relatively expensive. For the diagnosis of appendicitis, US should be the first-line imaging modality for children and pregnant women, except when the observation was interfered by the factors such as intestinal gas and overweight or obese patients [20]. In this study, the sensitivity and specificity of US diagnosing the acute appendicitis were 82.67% and 89.93%, respectively. It was reported that the sensitivity of ultrasound in diagnosing appendicitis ranged from 69.2–92.0%, and specificity ranging from 81.0–97.0% [15]. The effectiveness of different studies on the diagnosis of appendicitis varies, which may be related to the pathological types of the appendix and the selection of ultrasound signs. Different pathological types of appendicitis are closely related to its complications, surgical timing and prognosis, and delayed management may lead to severe complications such as perforation of the appendix and spread of infection. US may evaluate the pathological types of appendicitis before surgery, which is helpful for clinicians making decisions. It has been reported that ultrasonography is of great value in distinguishing acute simple appendicitis from complicated appendicitis [21], while there are a few of studies focusing on the association between ultrasonic description and pathological classification of acute appendicitis in children.

In this study, the diagnostic accuracy of ultrasonography for different pathological types of appendicitis was 78.95% (30/38) for acute simple appendicitis, 81.97% (50/61) for acute suppurative appendicitis and 92.16% (47/51) for acute gangrenous appendicitis. The diagnosis accuracy of acute suppurative appendicitis and acute gangrenous appendicitis is relatively high, probably because US can observe inflammation affecting a wide range and deep level. Acute complicated appendicitis usually manifested as a large quantity of inflammatory exudate, deep and large ulcers of the appendiceal wall. The lesions even involve of the whole layer of the appendix wall, and some of them are combined with abscesses around the appendix.

The typical ultrasonography of acute complicated appendicitis of acute complicated appendicitis manifestations are thickening of the appendix, thickening of the tube wall, dilation of the lumen, coprolites in part of the lumen, effusion and lymph node enlargement around the appendix in part, making it easily identifiable. However, the diagnostic accuracy of ultrasound in patients with acute simple appendicitis was relatively low (78.95%) as the inflammatory in patients with acute simple appendicitis is limited to the mucosa and submucosa, with less inflammatory exudate, less obvious thickening of the appendix wall, and it is difficult to distinguish the appendix from the surrounding normal mesenteric tissues and intestinal echoes. In this study, though these methods all have certain limitations, when US and PAS and CRP were combined for diagnosing acute appendicitis, the sensitivity was 99.33% (149/150) and 98.21% (110/112) for acute complicated appendicitis, which could be of great help to the clinicians in making clinical decisions.

However, this study has some defects. For the selection of the cutoff value, limited by the length of the article, we selected only the cutoff value corresponding to the maximum Youden index. In addition, this study only analyzed cases of pediatric patients with acute abdominal pain and a clear discharge diagnosis, which may have limited the scope of inclusion, and the cases selected in this study were 268, these problems could be solved if we consider more cases and more center.

In conclusion, the combination of PAS, CRP and US plays an important role in the diagnosis of acute appendicitis and the distinction between acute simple appendicitis and acute complicated appendicitis. Ultrasonography has certain value in diagnosing of acute appendicitis and identifying different pathological types.

Declarations

CONFLICT OF INTEREST

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding authors.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by the Ethics Committee of The First Affiliated Hospital of Guangxi Medical University. Written informed consent to participate in this study was provided by the participants' legal guardian/next of kin.

AUTHOR CONTRIBUTIONS

J-YH and Y-GL: conception and design of the research. M-HL, CS, WL and J-HL: acquisition of data. J-BC and M-HL: analysis and interpretation of the data. HH and WL: statistical analysis. HH and M-HL: writing of the manuscript. Y-GL: critical revision of the manuscript for intellectual content. All authors read and approved the final draft.

FUNDING

No authors received any funding resource.

References

1. Rothrock SG, Pagane J (2000) Acute appendicitis in children: emergency department diagnosis and management. *Ann Emerg Med* 36(1):39–51. 10.1067/mem.2000.105658
2. Téoule P, Laffolie J, Rolle U, Reissfelder C (2020) Acute Appendicitis in Childhood and Adulthood. *Dtsch Arztebl Int* 117(45):764–774. 10.3238/arztebl.2020.0764
3. Shafi S, Aboutanos M, Brown CV et al (2014) American Association for the Surgery of Trauma Committee on Patient Assessment and Outcomes. Measuring anatomic severity of disease in emergency general surgery. *J Trauma Acute Care Surg* 76(3):884–887. 10.1097/TA.0b013e3182aafdba
4. Di Saverio S, Podda M, De Simone B et al (2020) Diagnosis and treatment of acute appendicitis: 2020 update of the WSES Jerusalem guidelines. *World J Emerg Surg* 15(1):27. 10.1186/s13017-020-00306-3
5. Snyder MJ, Guthrie M, Cagle S (2018) Acute Appendicitis: Efficient Diagnosis and Management. *Am Fam Physician* 98(1):25–33
6. Almaramhy HH (2017) Acute appendicitis in young children less than 5 years: review article. *Ital J Pediatr* 43(1):15. 10.1186/s13052-017-0335-2
7. Sağ S, Basar D, Yurdadoğan F, Pehlivan Y et al (2022) Comparison of Appendicitis Scoring Systems in Childhood Appendicitis. *Turk Arch Pediatr* 57(5):532–537. 10.5152/TurkArchPediatr.2022.22076
8. de Dios O, Gavela-Pérez T, Aguado-Roncero P et al (2018) C-reactive protein expression in adipose tissue of children with acute appendicitis. *Pediatr Res* 84(4):564–567. 10.1038/s41390-018-0091-z
9. Zouari M, Louati H, Abid I et al (2018) C-reactive protein value is a strong predictor of acute appendicitis in young children. *Am J Emerg Med* ;36(7):1319–1320. doi: 101016/j.ajem.2017.11.067
10. Gonzalez DO, Lawrence AE, Cooper JN et al (2018) Can ultrasound reliably identify complicated appendicitis in children? *J Surg Res* 229:76–81. 10.1016/j.jss.2018.03.012
11. Gongidi P, Bellah RD (2017) Ultrasound of the pediatric appendix. *Pediatr Radiol* 47(9):1091–1100. 10.1007/s00247-017-3928-4
12. Di Saverio S, Birindelli A, Kelly MD et al (2016) WSES Jerusalem guidelines for diagnosis and treatment of acute appendicitis. *World J Emerg Surg* 11:34 Published 2016 Jul 18. 10.1186/s13017-016-0090-5
13. Samuel M (2002) Pediatric appendicitis score. *J Pediatr Surg* vol 37(6):877–881. 10.1053/jpsu.2002.32893
14. Howell JM, Eddy OL, Lukens TW et al (2010) Clinical policy: critical issues in the evaluation and management of emergency department patients with suspected appendicitis. *Ann Emerg Med* 55:71–116. 10.1016/j.annemergmed.2009.10.004
15. Lone NA, Shah M, Wani KA, Peer GQ (2006) Modified Alvarado score in diagnosis of acute appendicitis. *Ind J Pract Dr* 3(2):5–6
16. Yu CW, Juan LI, Wu MH et al (2013) Systematic review and meta-analysis of the diagnostic accuracy of procalcitonin, C-reactive protein and white blood cell count for suspected acute appendicitis. *Br J Surg* 100(3):322–329. 10.1002/bjs.9008
17. Kim JJY, Dobson BH, Ng LH (2020) QUEST Collaboration. Can normal inflammatory markers rule out acute appendicitis? The reliability of biochemical investigations in diagnosis. *ANZ J Surg* 90(10):1970–1974. 10.1111/ans.15559
18. Ates U, Bahadir K, Ergun E et al (2020) Determination of pentraxin 3 levels in diagnosis of appendicitis in children. *Pediatr Int* 62(5):624–628. 10.1111/ped.14131
19. Anand S, Krishnan N, Jukić M et al (2022) Utility of Red Cell Distribution Width (RDW) as a Noninvasive Biomarker for the Diagnosis of Acute Appendicitis: A Systematic Review and Meta-Analysis of 5222 Cases. *Diagnostics (Basel)* 12(4):1011. 10.3390/diagnostics12041011
20. Eng KA, Abadeh A, Ligocki C et al (2018) Acute Appendicitis: A Meta-Analysis of the Diagnostic Accuracy of US, CT, and MRI as Second-Line Imaging Tests after an Initial US. *Radiology* 288(3):717–727. 10.1148/radiol.2018180318
21. Gongidi P, Bellah RD (2017) Ultrasound of the pediatric appendix. *Pediatr Radiol* 47(9):1091–1100. 10.1007/s00247-017-3928-4

Figures

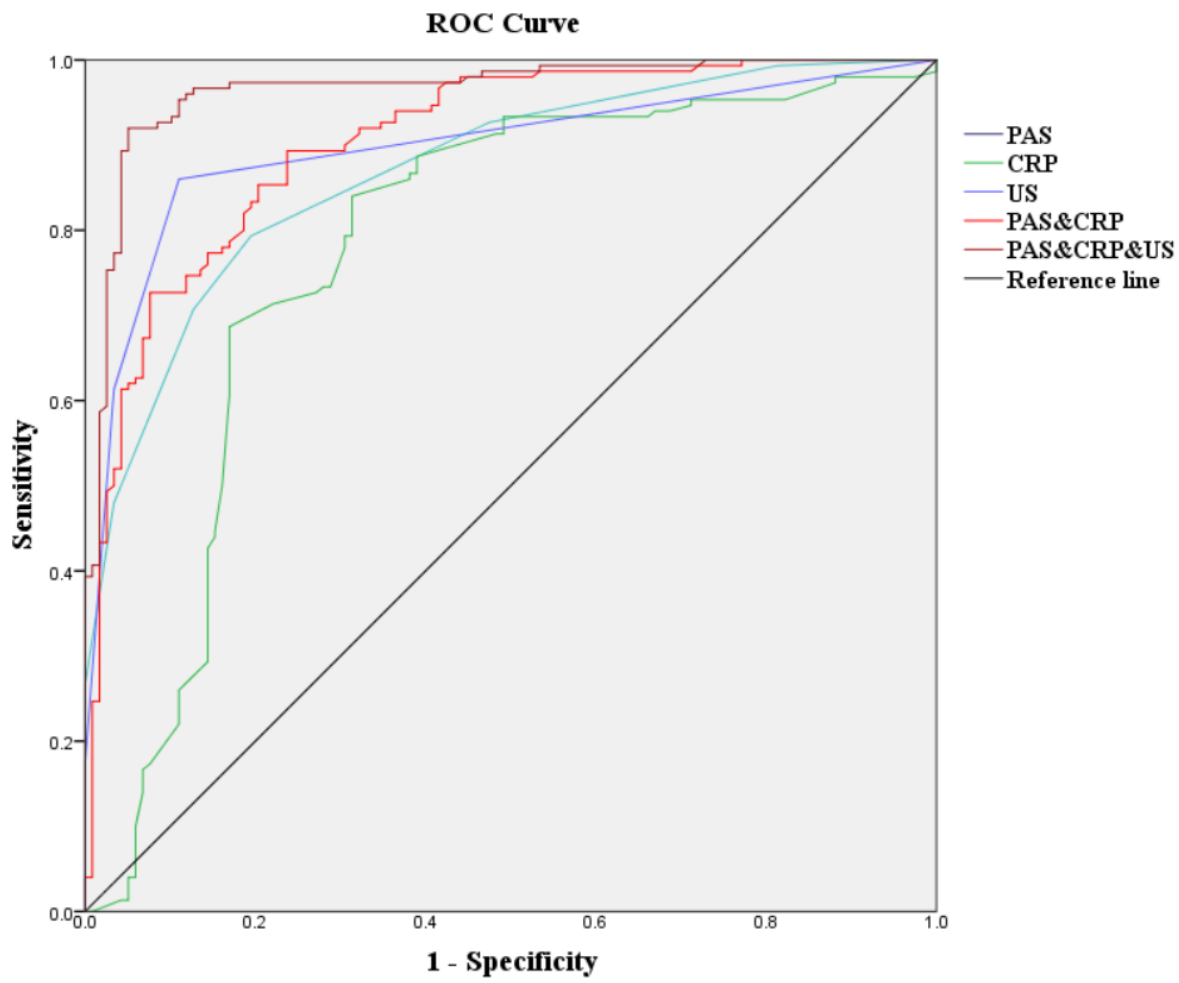


Figure 1

ROC curve of Pediatric appendicitis score and CRP for diagnosing acute appendicitis

ROC Curve

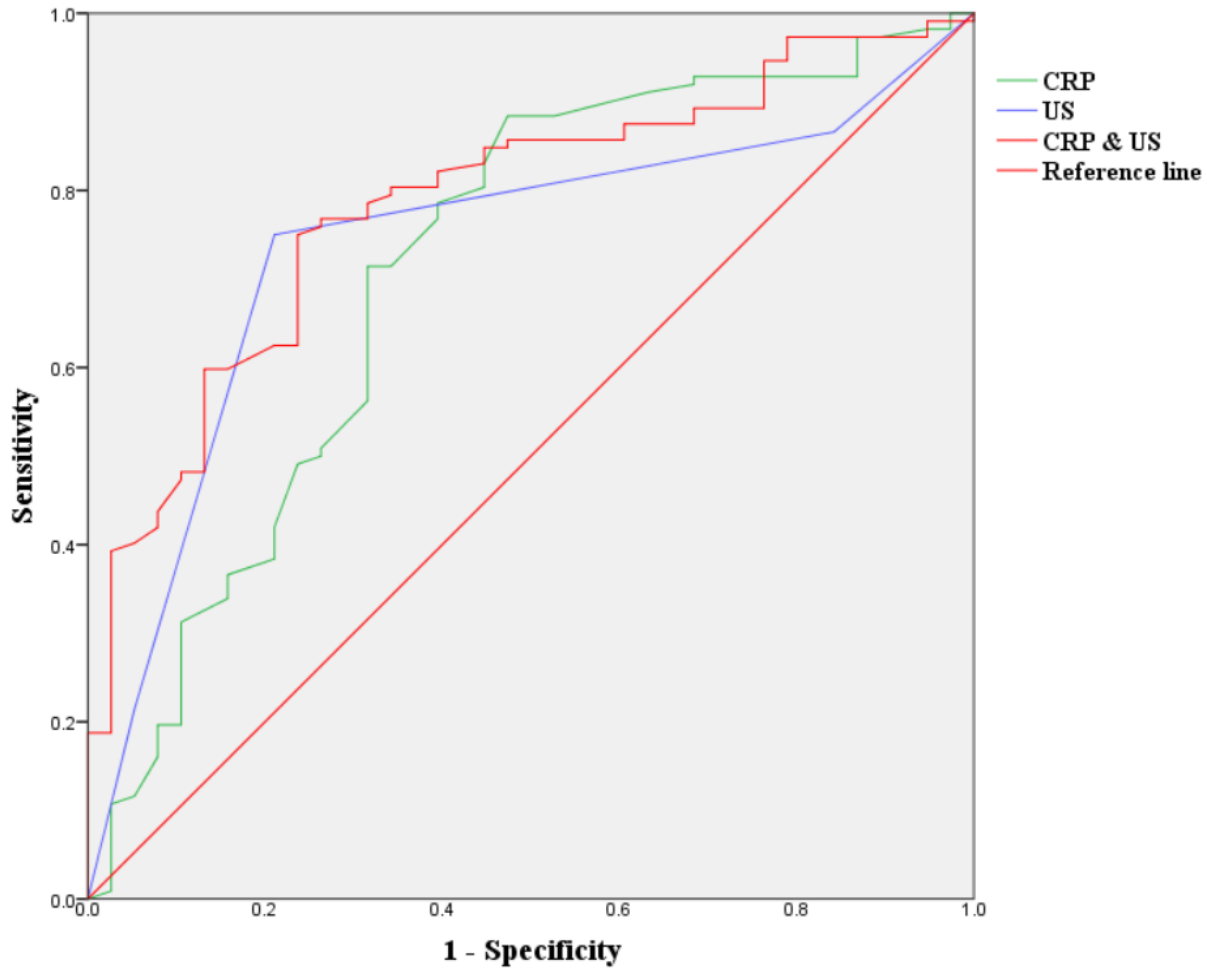


Figure 2

ROC curve of PAS and CRP for diagnosing acute complicated appendicitis

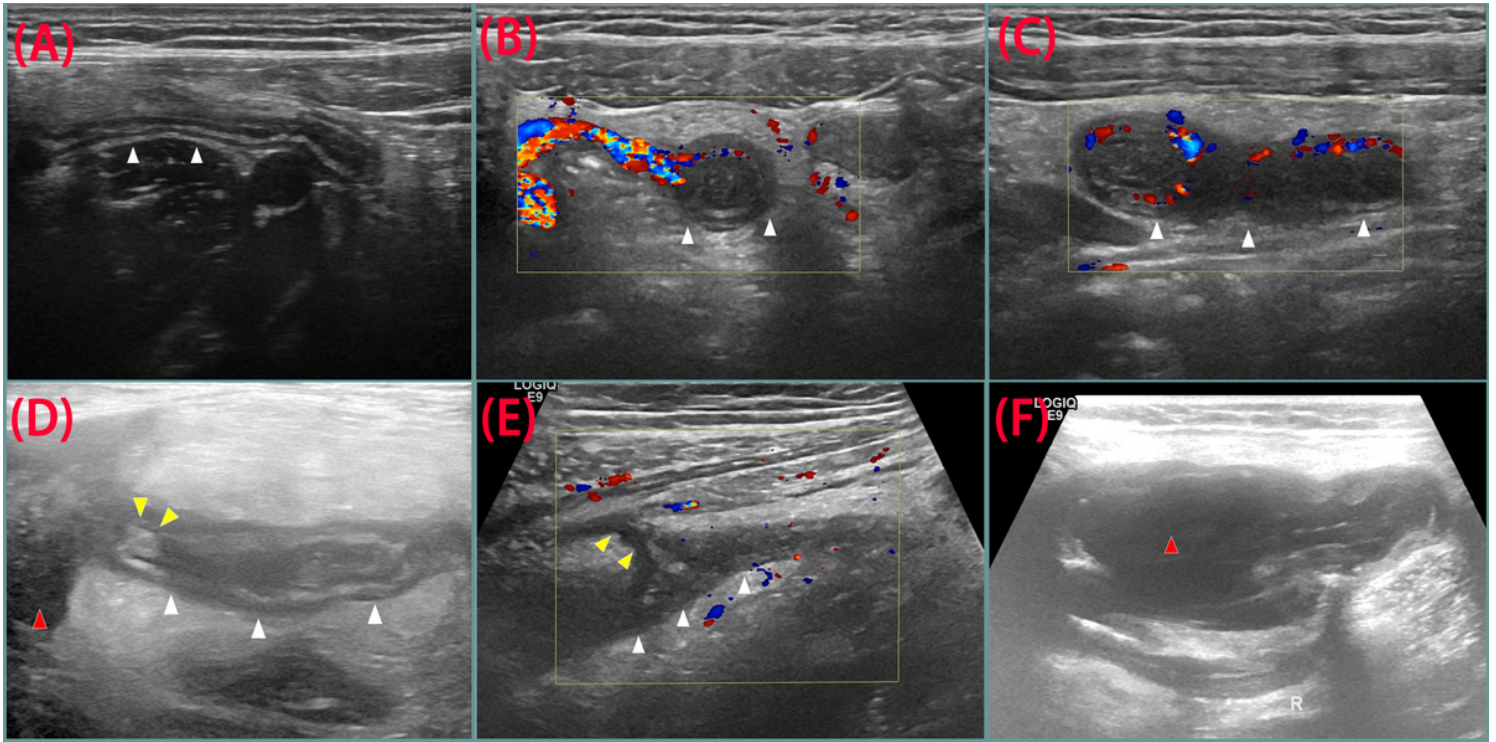


Figure 3

Ultrasonographic manifestations of various types of acute appendicitis

(A), Ultrasonography of simple appendicitis (longitudinal section): the white arrow, clear hierarchical boundaries of appendiceal wall

(B) and (C), Ultrasonography of suppurative appendicitis (transverse section): the white arrow, appendiceal wall

(C), Ultrasonography of suppurative appendicitis (longitudinal section): the white arrow, appendiceal wall

(D), Ultrasonography of suppurative appendicitis with stercolith: yellow arrow, stercolith; white arrow, appendix ; red arrow, cecum

(E), Ultrasonography of gangrenous perforative appendicitis: red arrow, perforation; white arrow: appendix

(F), Ultrasonography of gangrenous appendicitis with periappendiceal abscess: red arrow, appendiceal cavity