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The predictive value of the C-reactive protein/albumin ratio in adult patients with complicated appendicitis

Abstract

Objectives: The purpose of this study was to analyze the role of C-reactive protein/albumin ratio (CRP/ALB) in the diagnosis of complicated appendicitis in adults.

Methods: A retrospective analysis of 202 patients with acute appendicitis admitted to the Emergency Department of Weifang People's Hospital between January 2021 and December 2022 was conducted. Patients were classified into complicated appendicitis group (CA) and non-complicated appendicitis group (NCA) based on postoperative pathological diagnosis, and the two groups were compared in terms of preoperative age, gender, white blood cell count (WBCC), C-reactive protein/albumin ratio (CRP/ALB), serum sodium (Na), and fibrinogen (FIB).

Results: The 202 cases of acute appendicitis in this study, 36.6 % (n=74) were CA. Multivariate logistic regression analysis showed that CPR/ALB (p≤0.001), FIB (p<0.001), and Na (p=0.011) were risk factors for complicated appendicitis. The results of receiver operating characteristic (ROC) analysis, conducted to evaluate the role of CRP/ALB, Na, and FIB in detecting CA, showed that the area under the curve (AUC) of CRP/ALB was 0.871, which was higher than that of FIB and Na. CRP/ALB ratio ≥1.04 was an important indicator for predicting complicated appendicitis, with a sensitivity of 78.2 % and specificity of 84.7 %.

Conclusions: CRP/ALB ratio can serve as a good indicator for predicting complicated appendicitis.

Keywords: complicated appendicitis; C-reactive protein/albumin; serum sodium; fibrinogen; adult; predictive factors

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Introduction

Acute appendicitis (AA) is one of the most common acute abdominal emergencies in general surgery [1]. As a frequently encountered acute abdominal symptom, the lifetime risk of AA in men and women is 8.6 and 6.9 %, respectively [2]. According to the pathological type, AA can be classified into two categories: non-complicated appendicitis (NCA) and complicated appendicitis (CA), where NCA includes acute simple and suppurative appendicitis, while CA involves appendiceal necrosis, perforation or periappendiceal abscess [3]. About 3.8–5.0 % of AA patients develop into CA due to delayed treatment, rapid progression of disease or ineffective anti-infective treatment, resulting in severe intra-abdominal infection [4]. Complications related to appendectomy, prolonged hospitalization and secondary surgery are suggested to be associated with acute CA [5]. Although surgical treatment is effective for CA, it may lead to postoperative complications such as adhesive ileus, hemorrhage, and fecal leakage. With the development of digestive endoscopy, endoscopic retrograde appendicitis treatment (ERAT) can be a choice for NCA patients. ERAT has advantages over appendectomy, including no skin incision, organ preservation, reduced postoperative pain, early oral intake, faster recovery, fewer postoperative complications and shorter hospitalization [6]. However, how to accurately and early identify acute CA and NCA is a major challenge. Clinical presentation, Alvarado score and ultrasonography can be helpful for diagnosing AA, but it is difficult to determine the type of appendicitis. In about half of the patients, ultrasonography may fail to detect the appendix clearly, and computed tomography (CT) is limited by radiation and high cost [7]. Therefore, various common inflammatory markers, such as white blood cell count, neutrophil count and mean platelet volume, have been used to predict acute perforated appendicitis due to their simplicity and feasibility [8, 9]. The C-reactive protein/albumin ratio (CRP/ALB) is a novel inflammation-based prognostic score that is related to the severity of inflammation [10]. Previous reports [11, 12] have shown that CRP/ALB is a marker for predicting the surgical mortality of necrotizing enterocolitis in newborns and the prognosis of septicemia in children. CRP/ALB is related to the

disease progression of various infectious diseases and has been widely applied in prognostic prediction of diseases such as pancreatic tumors, colon cancer, rectal cancer [13–15]. Hyponatremia is a common electrolyte disturbance, and studies have shown that it is associated with increased incidence and mortality in the perioperative period [16]. In inflammatory cases, the occurrence of hyponatremia may involve the process of inflammatory cytokines and antidiuretic hormone (ADH) secretion. Inflammation leads to an increase in interleukin (IL)-1b and IL-6 levels, which stimulate ADH release, ultimately resulting in hyponatremia [17, 18]. According to some studies, an elevated level of fibrinogen (FIB) is associated with the severity of acute appendicitis [19]. To further investigate the predictive value of CRP/ALB ratio, serum Na and FIB for CA, we conducted the following study.

Materials and methods

A retrospective analysis was conducted using a sample of patients aged 18 years and above who underwent appendectomy at the Emergency and General Surgery Department of Weifang People's Hospital between January 2021 and December 2022, all of whom were diagnosed with acute appendicitis.

Inclusion criteria were as follows: (1) age of 18 years or above, (2) previous appendectomy at our hospital, (3) pathologically confirmed acute appendicitis, and (4) approved by the hospital's Ethics Committee.

Patients who underwent elective surgery or those with infectious diseases, malignant tumors, liver or kidney disease, chronic inflammatory diseases, and hematologic disorders were excluded from the study. Additionally, participants who underwent appendectomy for other reasons (such as malignant tumors) but were pathologically confirmed not to have acute appendicitis were also excluded. The surgical procedures included open or laparoscopic surgery, and postoperative specimens were examined by the pathology department of Weifang People's Hospital. All patient data were obtained from the hospital's electronic medical record system.

Laboratory parameters (white blood cell count, serum sodium, fibrinogen, and C-reactive protein/albumin ratio), age, gender, and pathological classification of acute appendicitis were collected. Based on the postoperative pathological examination results of acute appendicitis, gangrenous/perforated appendicitis was classified as complicated appendicitis, while simple and suppurative appendicitis were classified as uncomplicated appendicitis.

Statistical methods

All data were organized and stored in an electronic database (Microsoft Excel) and analyzed using SPSS 25.0. The curve graphs were plotted utilizing GraphPad Prism 9.5. Quantitative variables were reported as mean ± standard deviation or median, interquartile range, while categorical variables were presented as counts and percentages. The Student's t-test and Mann-Whitney U test were used for continuous data analysis, and the Pearson chi-square test was used for categorical variables. Multiple logistic regression analysis was conducted to identify independent factors associated with complex appendicitis. ROC curve analysis and the area under the curve (AUC) were used to identify independent predictors of complex appendicitis and determine the optimal cut-off point for diagnosing complex appendicitis. A p-value of <0.05, a 95 % confidence interval (95 % CI), and a 5 % margin of error were considered statistically significant.

Results

During the study period, a total of 236 patients who underwent appendectomy were collected. Based on the inclusion and exclusion criteria, 202 patients were finally included in the study, among whom 130 (64.4 %) were male and 72 (35.6 %) were female. Of the 202 patients, data showed that 74 (36.6 %) were found to have complicated appendicitis (CA), while the remaining 128 (63.4 %) had non-complicated appendicitis (NCA). The mean age of the 202 patients was 43 (31;57). When the patients were assessed separately, the mean age of CA and NCA patients were 46.5 (33.75;59.75) and 39.5 (30;57) (p=0.303). The mean serum Na level of CA patients was lower than that of NCA patients, and the mean levels of FIB and CPR/ALB were significantly higher in the CA group than in the NCA group (Table 1).

Multivariable logistic regression analysis was performed using two statistically significant variables between groups of NCA=0 and CA=1 patients as independent variables, with the type of acute appendicitis as the dependent variable. The analysis revealed that CPR/ALB (p<0.001), FIB (p<0.001), and serum Na (p=0.011) were independent risk factors for CA (Table 2).

The present study performed ROC curve analysis to determine the diagnostic value of CRP/ALB, FIB, and serum Na in CA. The AUC of CRP/ALB was 0.871, with a critical value of 1.04, sensitivity of 78.2 %, and specificity of 84.7 % (p≤0.001, [95 % CI, 0.816–0.925]). FIB yielded an AUC of

Table 1: General data comparison between the NCA group and CA group ($\overline{X} \pm$ S, median (IQR)).

	NCA n=128	CA n=74	p-Value
Age	39.5 (30;57)	46.5 (33.75;59.75)	0.303
Gender[a]			
Male	77 (60.2 %)	53 (71.6 %)	0.001
Female	51 (39.8 %)	21 (28.4 %)	
WBCC, ×10⁹/L	11.49 ± 3.68	12.92 ± 4.31	0.034
FIB, g/L	3.67 ± 0.96	4.82 ± 1.27	<0.001
CRP/ALB	0.25 (0.06;0.67)	2.55 (1.39;4.05)	<0.001
Na, mEq/L	138.99 ± 2.89	136.35 ± 4.13	<0.001

[a]Count and percentage; WBCC, white blood cell count; FIB, fibrinogen; CRP/ALB, C-reactive protein/albumin; Na, serum sodium.

Table 2: Multivariate logistic regression analysis.

	β	Standard error	p-Value	OR	OR 95 % CI
Na	−0.172	0.068	0.011	0.842	0.738–0.962
FIB	1.063	0.693	<0.001	2.894	1.799–4.658
CRP/ALB	1.212	0.227	<0.001	3.361	2.156–5.241

Na, serum sodium; FIB, fibrinogen; CRP/ALB, C-reactive protein/albumin.

Table 3: ROC results summarized by AUC.

	AUC	Standard error	p-Value	95 % CI
Na	0.68	0.037	<0.001	0.602–0.759
FIB	0.766	0.034	<0.001	0.700–0.832
CRP/ALB	0.871	0.028	<0.001	0.816–0.925

Na, serum sodium; FIB, fibrinogen; CRP/ALB, C-reactive protein/albumin.
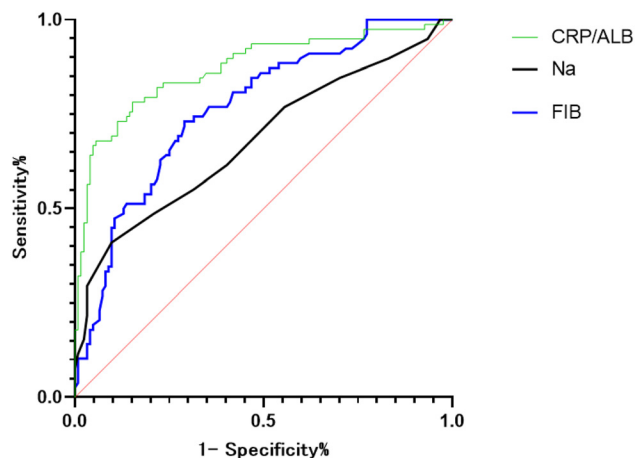
Figure 1: ROC curves.

76.6 %, with a critical value of 4.03 g/L, sensitivity of 73.1 %, and specificity of 71.0 % (p<0.0001, [95 % CI, 0.700–0.832]). The AUC of serum Na was 68.0 %, with a critical value of 135 mEq/L, sensitivity of 40.0 %, and specificity of 90.3 % (p≤0.001, [95 % CI, 0.602–0.759]). CRP yielded an AUC of 0.867, with a critical value of 81.55 mg/L, sensitivity of 67.9 %, and specificity of 94.4 % (p≤0.001, [95 % CI, 0.813–0.922]) (Table 3, Figure 1).

Discussion

The treatment of acute appendicitis has evolved significantly in recent years, with clinicians having access to a wider range of treatment options. Recent research suggests that most cases of acute uncomplicated appendicitis can be treated using an antibiotic-first approach [20, 21]. Antibiotic therapy alone has been shown to offer several advantages

for patients, including avoiding surgical scars, postoperative pain, and a quicker recovery [22]. With the development of digestive endoscopy, less invasive procedures, such as endoscopic retrograde appendicitis therapy (ERAT), have become safe and effective options for the treatment of non-complicated appendicitis. Liu et al. conducted a multicenter retrospective study that analyzed the efficacy and safety of ERAT on treating non-complicated appendicitis in 33 patients, of which 32 experienced immediate relief of abdominal pain [23]. Research has shown that the appendix serves as not only a lymphatic organ with immune function but also as a site for immune replication and regeneration and secretes various digestive enzymes and gastrointestinal hormones. Furthermore, it helps maintain a balance of the intestinal microbiota and reduces the risk of colorectal cancer [24, 25]. For patients with non-complicated appendicitis, a combination of antibiotic and ERAT therapy provides more benefits to long-term quality of life and aligns with patients' cosmetic requirements. For complicated appendicitis, traditional surgical intervention remains the primary option. However, research has shown that there is a high negative-appendectomy rate of more than 15 % [26]. As such, prompt identification of the type of acute appendicitis is particularly important for selecting the appropriate treatment strategy.

CRP/ALB is considered as a relevant biological marker reflecting microvascular permeability [27]. Several studies have shown that the CRP/ALB ratio can indicate the degree of inflammation and prognosis of inflammatory bowel disease and pancreatitis [28–30], but there is no report on using CRP/ALB as a diagnostic marker for adult complicated appendicitis. Hu et al. demonstrated that CRP/ALB is a reliable biomarker for complicated appendicitis in children, and patients with a CRP/ALB ratio ≥1.39 are more likely to suffer from complicated appendicitis [31]. Serum Na and FIB, as simple, inexpensive and widely used laboratory tests, have been reported to be helpful in determining the diagnosis of necrotizing soft tissue infections and predicting the mortality of these patients with low serum sodium [32]. Preoperative hyponatremia has been shown to be associated with an increase in perioperative morbidity and mortality [16], and it was found to be an important potential indicator for predicting rectal anastomotic leakage in the report of Alsaleh et al. [33] Acute appendicitis is usually associated with systemic inflammatory response, often leading to coagulation activation, and FIB, as an indicator of pro-inflammatory state, increases several times and acts as a regulator in several pathological conditions such as inflammation after infection or injury, tissue repair or disease-related endothelial damage [34, 35].

In this study, a multiple logistic regression analysis revealed that CPR/ALB, FIB, and Na were independent risk factors for CA. Different cut-off values for CRP/ALB, FIB, and Na levels were established as predictive factors for CA in ROC analysis. CPR/ALB, as a novel inflammatory marker, demonstrated good diagnostic efficacy for CA when the ratio exceeded 1.04. There was no significant difference between using the commonly used cut-off values for low sodium and high fibrinogen levels and the cut-off values identified in this study. We believe that using the widely adopted cut-off values would facilitate the implementation of routine clinical practice. However, the use of cut-off values derived from ROC analysis enhanced the sensitivity and accuracy of CA diagnosis.

Our study has some limitations. Firstly, as our data was retrospectively collected, it only includes patients who underwent appendectomy and does not investigate patients who received conservative treatment. Additionally, this was a small sample, single-center study. Therefore, further validation is required through large-scale prospective studies with multiple centers. Furthermore, potential confounding factors of cases occurring during the COVID-19 pandemic, such as reduced number of patients receiving surgical treatment, may have artificially lowered our number of complication-free cases.

Conclusions

This study aimed to identify predictive factors and indicators of complicated appendicitis through a retrospective analysis. In the adult population, statistically significant results were found indicating that patients with acute appendicitis who have a CRP/ALB ratio ≥1.04, hyponatremia, or hyperfibrinogenemia are more likely to develop complicated appendicitis. Additionally, by combining clinical symptoms and other diagnostic aids, clinicians can accurately diagnose complicated appendicitis. In conclusion, our study highlights the predictive value of CRP/ALB in complicated appendicitis.

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