ORIGINAL PAPER

DOI: http://dx.doi.org/10.15403/jgld-7029

Hemogram-derived Ratios in the Prognosis of Acute Appendicitis

Florin Vasile Mihaileanu[1], Vlad Dumitru Brata[2], Razvan Ciocan[1], Bogdan Stancu[1], Octavian Andercou[1], Caius Breazu[3,4,5], Claudia Diana Gherman[6], Julia Marton[7], Daniel Corneliu Leucuta[8], Traian Adrian Duse[9], Stefan Lucian Popa[10], Dinu Iuliu Dumitrascu[7]

1) Dept. of Surgery, Emergency County Hospital Cluj, Iuliu Haţieganu University of Medicine and Pharmacy, Cluj-Napoca; 2) Dept. of Gastroenterology, Prof. Dr. Octavian Fodor Regional Institute of Gastroenterology and Hepatology, Cluj-Napoca; 3) 1st Dept. of Anesthesia and Intensive Care, Iuliu Haţieganu University of Medicine and Pharmacy, Cluj-Napoca; 4) Dept. of Anesthesia and Intensive Care, Cluj County Emgency Clinical Hospital, Cluj-Napoca; 5) Research Association in Anesthesia and Intensive Care (ACATI), Cluj-Napoca; 6) Dept. of Surgery-Practical Abilities, Iuliu Haţieganu University of Medicine and Pharmacy, Cluj-Napoca; 7) Dept. of Anatomy and Embryology, Iuliu Haţieganu University of Medicine and Pharmacy, Cluj-Napoca; 8) Dept. of Medical Informatics and Biostatistics, Iuliu Haţieganu University of Medicine and Pharmacy, Cluj-Napoca; 9) Dept. of Surgery, Prof. Dr. Octavian Fodor Regional Institute of Gastroenterology and Hepatology, Cluj-Napoca; 10) 2nd Dept. Iuliu Hatieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania

Address for correspondence:
Vlad Dumitru Brata
Prof. Dr. Octavian Fodor Regional Institute of Gastroenterology and Hepatology, Cluj-Napoca, Romania
brata.vladdumitru@elearn.umfcluj.ro

Received: 10.03.2026
Accepted: 26.05.2026

ABSTRACT

Background & Aims: Early identification by gastroenterologists of peritonitis in acute appendicitis may support timely decision-making when clinical assessment and imaging are equivocal. The aim of this study was to assess the diagnostic and predictive value of routinely available laboratory parameters and systemic inflammatory indices in identifying peritonitis among patients undergoing surgery for acute appendicitis. By integrating clinical features, biochemical markers and composite hematological ratios, this study seeks to contribute to improved risk stratification and early decision-making in patients with acute appendicitis.
Methods: We conducted a single-center retrospective observational study of adults (≥18 years) undergoing appendectomy for acute appendicitis (July 2023–July 2024). Patients were stratified by intraoperatively confirmed peritonitis. Admission biomarkers and complete hemogram–derived indices were evaluated using ROC analysis (AUC; Youden cut-offs). Multivariable logistic regression models were adjusted for age, gender, time from symptom onset to surgery, and Alvarado score.
Results: Among the 99 patients included, 52 (52.5%) had peritonitis. Compared with patients without peritonitis, those with peritonitis had a higher median age, body mass index (BMI), Alvarado score, and C-reactive protein (CRP) level. CRP showed the highest discriminatory ability for identifying peritonitis (AUC=0.713, 95%CI: 0.613–0.813), with a cut-off value of 15.1 mg/L, corresponding to a sensitivity of 70.6% and a specificity of 70%. Hemogram-derived inflammatory indices demonstrated moderate discriminatory performance for predicting peritonitis, including the monocyte-to-lymphocyte ratio (MLR; AUC=0.680; cut-off ≥0.653), eosinophil count (AUC=0.663; cut-off 0.035×10^9/L) for predicting the absence of peritonitis, the systemic inflammation response index (SIRI; AUC=0.657; cut-off ≥7.42), and the neutrophil-to-lymphocyte ratio (NLR; AUC=0.647; cut-off ≥10.855). In adjusted models, MLR ≥0.653 (aOR=6.92, 95%CI: 2.55–21.21), SIRI ≥7.42 (aOR=6.89, 95%CI: 2.46–22.29), and NLR ≥10.855 (aOR=5.88, 95%CI: 2.16–18.13) were associated with increased odds of peritonitis, whereas eosinophil count $\geq0.035\times10^9$/L was inversely associated with peritonitis (aOR=0.22, 95%CI: 0.08–0.54).
Conclusions: Hemogram-derived inflammation indices, particularly MLR, SIRI, and NLR, are independently associated with intraoperative peritonitis and may complement CRP for preoperative risk stratification. Prospective multicenter validation is warranted to confirm thresholds and clinical utility.

Key words: acute appendicitis – peritonitis – complete blood count – inflammatory biomarkers – neutrophil-to-lymphocyte ratio – monocyte-to-lymphocyte ratio – systemic inflammation response index – risk stratification.

Abbreviations: AISI: aggregate index of systemic inflammation; ALP: alkaline phosphatase; ALT: alanine aminotransferase; AST: aspartate aminotransferase; AUC: area under the curve; aOR: adjusted odds ratio; BMI: body mass index; CI: confidence interval; CRP: C-reactive protein; CT: computed tomography; dNLR: derived neutrophil-to-lymphocyte ratio; GGT: gamma-glutamyl transferase; INR: international normalized ratio; IQR: interquartile range; LMR: lymphocyte-to-monocyte ratio; MLR: monocyte-to-lymphocyte ratio; NLR: neutrophil-to-lymphocyte ratio; NPR: neutrophil-to-platelet ratio; OR: odds ratio; PLR: platelet-to-lymphocyte ratio; PT: prothrombin time; RDW-CV: red cell distribution width - coefficient of variation; ROC: receiver operating characteristic; SII: systemic immune-inflammation index; SIRI: systemic inflammation response index; STROBE: strengthening the reporting of observational studies in epidemiology.

INTRODUCTION

Acute appendicitis represents one of the most frequent emergencies worldwide and a major cause of acute abdomen requiring urgent action. Although early diagnosis and timely therapy, including appendectomy, are generally associated with favorable outcomes, delayed presentation or progression of inflammation may lead to severe complications such as peritonitis, abscess formation, or sepsis, which considerably increase postoperative morbidity and healthcare costs [1].

Identifying patients at risk of complicated appendicitis before surgery is therefore clinically important, as it may support timely decision-making and improve surgical outcomes. Current diagnostic approaches in suspected appendicitis integrate clinical assessment, scoring systems (such as the Alvarado score), laboratory findings and imaging, most commonly ultrasound and abdominal tomography (CT) [2, 3]. However, ultrasound is highly operator-dependent, and diagnostic uncertainty may persist despite imaging. Consequently, reliance on imaging or clinical parameters alone may delay intervention in high-risk patients.

These tools have variable sensitivity and specificity, especially in early or atypical presentations. Laboratory markers including leukocyte count, neutrophil percentage and C-reactive protein (CRP) are commonly used to evaluate the inflammatory status, but their discriminative performance in predicting disease severity remains limited [4, 5]. Furthermore, current evidence suggests that inflammatory marker-based models may offer improved predictive capabilities compared to imaging alone in certain clinical contexts.

Recent evidence suggests that systemic inflammatory indices derived from complete blood count parameters, such as the neutrophil-to-lymphocyte ratio (NLR), monocyte-to-lymphocyte ratio (MLR) and systemic immune-inflammation index (SII) may better reflect the balance between pro-inflammatory and immune-regulatory responses than isolated laboratory markers [6]. In both adult and pediatric appendicitis cohorts, NLR has been associated with complicated disease [6-8]. The lymphocyte-to-monocyte ratio (LMR) has also been proposed for distinguishing complicated from uncomplicated appendicitis [8]. Because these parameters are routinely available and inexpensive, in most emergency settings, they may offer a practical advantage over more advanced diagnostic techniques. Furthermore, their application could be particularly valuable when imaging results are inconclusive or delayed, or when clinical evaluation is hindered by confounding symptoms.

Therefore, the aim of this study was to assess the diagnostic and predictive value of routinely available laboratory parameters and systemic inflammatory indices in identifying peritonitis among patients undergoing surgery for acute appendicitis. By integrating clinical features, biochemical markers and composite hematological ratios, this study seeks to contribute to improved risk stratification and early decision-making in patients with acute appendicitis.

METHODS

We conducted a retrospective observational study including patients aged ≥18 years who underwent surgical intervention for acute appendicitis. Eligible cases were identified from the electronic records of the Clinical Emergency County Hospital of Cluj-Napoca, Romania over a predefined period from July 2023 to July 2024. Patients were retrieved from the hospital database using diagnostic coding corresponding to acute appendicitis. Only patients with intraoperative confirmation of appendicitis and a complete laboratory panel at admission were included.

Patients were excluded if they had: a history of malignancy; no intraoperative confirmation of appendicitis; incomplete laboratory data (leukocyte, neutrophil, lymphocyte, monocyte or platelet counts); or a known pre-existing hematologic, inflammatory, or infectious condition that could interfere with biomarker interpretation.

The study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of Iuliu Haţieganu University of Medicine and Pharmacy Cluj-Napoca (approval no. AVZ/167/06.09.2024). All patients were contacted and provided informed consent prior to inclusion in the study. Reporting followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines [9].

The primary outcome was the association between inflammatory biomarkers and the presence of peritonitis, as confirmed intraoperatively. A secondary objective of the study was to evaluate whether inflammatory biomarkers and composite hematological indices could be used to anticipate the progression of acute appendicitis toward peritonitis, with the goal of exploring their potential applicability in predictive modeling and early risk stratification.

Clinical and laboratory data were retrospectively extracted from medical records, including age, gender, body mass index (BMI), duration of symptoms, Alvarado score, imaging modality (ultrasound and/or CT), and type of surgical intervention (laparoscopic or open appendectomy). Intraoperative findings were documented from operative reports, including appendicitis subtype (catarrhal, phlegmonous or gangrenous), presence and type of peritonitis (localized or generalized), and associated complications (abscess or perforation). Laboratory parameters at admission included leukocyte count, neutrophils, lymphocytes, monocytes, platelets, C-reactive protein (CRP), hepatic enzymes, coagulation parameters, renal function, glucose, electrolytes, and other hematological indices. Inflammatory ratios were calculated as follows:

NLR (Neutrophil-to-Lymphocyte Ratio) = Neutrophils / Lymphocytes

MLR (Monocyte-to-Lymphocyte Ratio) = Monocytes / Lymphocytes

SIRI (Systemic Inflammation Response Index) = (Neutrophils × Monocytes) / Lymphocytes

SII (Systemic Immune-Inflammation Index) = (Platelets × Neutrophils) / Lymphocytes

NPR (Neutrophil-to-Platelet Ratio) = Neutrophils / Platelets

Considering the rapid pathophysiological progression of acute appendicitis, we controlled the temporal relationship between laboratory testing and intraoperative diagnosis. For each patient, laboratory parameters included in the analysis were those obtained at initial hospital presentation prior to

surgical intervention. The maximum elapsed time between blood sampling and intraoperative assessment of peritonitis was 4 hours. No repeat laboratory measurements were used for the primary analysis, and no cases required exclusion based on prolonged delay between laboratory assessment and surgery. This approach ensured that laboratory values reflected the inflammatory status as close as possible to the intraoperative findings.

Patients were stratified based on intraoperative presence or absence of peritonitis. Peritonitis was diagnosed intraoperatively based on direct surgical findings, defined by the presence of purulent or turbid peritoneal fluid, fibrinous exudates, and macroscopic signs of peritoneal inflammation. Some cases were associated with appendiceal perforation in gangrenous appendicitis, while others showed localized peritonitis without macroscopic perforation, attributed to bacterial translocation. Therefore, peritonitis was diagnosed independently of the presence or absence of appendiceal perforation.

The initial diagnosis was established intraoperatively based on direct surgical assessment.

Statistical Analysis

Categorical variables were presented as absolute and relative frequencies. Continuous data that did not follow a normal distribution were presented as medians and interquartile ranges (reported as quartile 1 – quartile 3). Comparisons between two independent groups concerning categorical variables were tested with chi-squared test or Fisher exact test, while data that was not following a normal distribution were tested with Wilcoxon rank-sum test. Receiver operator characteristic (ROC) curves, along with area under the curve (AUC), its 95% confidence interval, and the best cut-off values computed to maximize Youden index were presented, along with the corresponding sensitivity and specificity. To check the robustness of the univariate results, we built several multivariate logistic regression models, using the biomarkers with the best AUCs, and with their corresponding cutoffs, adjusted for age, sex, symptoms debut (above or below 12 hours), and Alvarado score. We checked the linearity of the continuous predictors with the logit using a generalized additive model, and we found that age and Alvarado scores had a nonlinear relationship. Thus, we dichotomized these variables prior to entering them in multivariate models. We chose the variables as clinically relevant possible confounders. We chose that the number of variables is about 5, to ensure that there are 10 events per variable, to prevent overfitting. All the models were checked for multicollinearity with variance inflation factors. The results of the models were presented as odds ratio, 95% confidence intervals (CI) and p-values. All statistical analyses were performed in R environment for statistical computing and graphics (R Foundation for Statistical Computing, Vienna, Austria), version 4.3.2.

RESULTS

A total of 99 patients were included in the analysis. The median age was 29 years (IQR: 22–45), and 50 patients (50.51%) were female. The median BMI was 24.88 kg/m^2 (IQR: 22.04–29.22). Only 30 patients (30.3%) underwent surgical intervention within 12 hours of symptom onset, whereas 69 (69.7%) after more than 12 hours; and 48 patients (48.5%) underwent surgery more than 24 hours after symptom onset. The median Alvarado score was 8 (IQR: 7–9). Imaging evaluation included ultrasound in 85 patients (85.9%) and CT in 43 patients (43.4%).

Laparoscopic appendectomy was performed in 93 cases (93.9%), while 6 patients (6.1%) required open surgery. Intraoperative findings revealed catarrhal appendicitis in 24 patients (24.2%), phlegmonous in 44 (44.4%), and gangrenous in 31 (31.3%). Adhesive syndrome was observed in 46 patients (46.5%). Peritonitis was present in 52 cases (52.5%), of which 40 (40.4%) were localized and 12 (12.1%) generalized. Appendiceal perforation was identified in 4 patients (4.0%). Pericecal and peritoneal abscesses were each reported in 1 patient (1.0%), with additional abscess localization in 2 cases (2.0%).

Postoperative evolution was generally favorable, with very low complication rates. Local complications were recorded in 2 patients (2.0%), including peri-incisional cellulitis and appendiceal stump bleeding requiring colonoscopic clipping, while 97 patients (98%) had no local complications. General postoperative complications were observed in 7 patients (7.1%), including postoperative ileus in 3 patients (3%), hepatic abscess in 1 patient (1%), intestinal infarction in 1 patient (1%), ureteral lithiasis requiring stenting in 1 patient (1%), and acute-on-chronic pancreatitis in 1 patient (1%). No general complications were reported in 92 patients. The complete demographic and clinical characteristics of the cohort are detailed in Table I.

Patients with peritonitis (n = 52) were significantly older than those without (36 vs. 25 years, p<0.001) and had a higher BMI (26.23 vs. 22.89 kg/m^2, p=0.008). The median Alvarado score was also higher in the peritonitis group (8 vs. 7, p=0.002). CRP levels were markedly elevated in patients with peritonitis (30 vs. 7.83 mg/L, p<0.001).

No significant differences were observed for aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), gamma-glutamyl transferase (GGT) or bilirubin. However, patients with peritonitis showed increased international normalized ratio (INR) (1.15 vs. 1.08, p=0.016), prolonged prothrombin time (PT) (13 vs. 12.2 s, p=0.018), and higher creatinine (0.9 vs. 0.78 mg/dL, p=0.014). Sodium levels were slightly lower in the peritonitis group (136.5 vs. 138 mmol/L, p=0.02).

Hematologically, patients with peritonitis had lower lymphocyte counts (1.29 vs. 1.6 $\times 10^9$/L, p=0.041), while eosinophils (p=0.005) and basophils (p=0.035) were significantly lower. RDW-CV was slightly higher in the peritonitis group (p=0.039), whereas platelet count did not differ significantly.

Systemic inflammatory indices were consistently higher in patients with peritonitis, including NLR (11.39 vs. 6.92, p=0.012), MLR (0.71 vs. 0.43, p=0.002), NPR (p=0.048), SIRI (p=0.007), and AISI (p=0.021). SII did not reach statistical significance (p=0.051), and neither did dNLR nor PLR.

Table I. Patients' characteristics

Characteristic		Number (N=99)
Median age (years- IQR)		29 (22 - 45)
Gender (M/F) (%)		49/50 (49.49)
Median BMI (kg/m^2)		24.88 (22.04 - 29.22)
Time until surgical intervention after onset of symptoms, n (%)	< 6 h	6 (6.06)
	6-12 h	24 (24.24)
	12-24 h	21 (21.21)
	> 24 h	48 (48.48)
Median Alvarado score, n (%)		8 (7 - 9)
Ultrasound diagnosis, n (%)		85 (85.86)
CT diagnosis, n (%)		43 (43.43)
Type of intervention, n (%)	Open	6 (6.06)
	Laparoscopic	93 (93.93)
Intraoperative appearance of appendicitis, n (%)	Catarrhal	24 (24.24)
	Phlegmonous	44 (44.44)
	Gangrenous	31 (31.31)
Adhesive syndrome/ adhesive block, n (%)		46 (46.46)
Presence of peritonitis, n (%)		52 (52.53)
Type of peritonitis, n (%)	None	47 (47.47)
	Generalized	12 (12.12)
	Localized	40 (40.4)
	Pericecal abscess	1 (1.01)
	Peritoneal abscess	1 (1.01)
	Perforation	4 (4.04)
	Other abscesses	2 (2.02)
Local complications, n (%)	Peri-incisional cellulitis	1 (1.01)
	Appendiceal stump bleeding- colonoscopic clipping	1 (1.01)
	No local complications	97 (97.98)
General complications, n (%)	Hepatic abscess	1 (1.01)
	Ileus	3 (3.03)
	Intestinal infarction	1 (1.01)
	Ureteral lithiasis- stenting	1 (1.01)
	No general complications	92 (92.93)
	Acute-on-chronic pancreatitis	1 (1.01)
Smoking (pack/years), n (%)		39 (39.39)
Diabetes, n (%)		3 (3.03)
Hypertension, n (%)		17 (17.17)
Heart failure, n (%)		3 (3.03)
Ischemic heart disease, n (%)		6 (6.06)

IQR: interquartile range reported as quartile 1 – quartile 3; BMI: body mass index; CT: computed tomography; n: number of cases.

Overall, patients with peritonitis exhibited a more pronounced systemic inflammatory response, higher severity scores, and subtle alterations in coagulation and renal parameters. These findings suggest an association between systemic inflammatory indices and the presence of peritonitis. Full laboratory comparisons are presented in Table II.

Among the evaluated biomarkers, CRP demonstrated the highest discriminative ability for peritonitis, with an AUC of 0.713 (95% CI: 0.613–0.813), sensitivity of 70.59%, and specificity of 70.00% at a cut-off value of 15.1 mg/L. MLR (predicting the presence of peritonitis) and eosinophil count (predicting absence of peritonitis) showed moderate performance, with AUCs of 0.680 (95% CI: 0.577–0.784), 0.663 (95% CI: 0.557–0.767), 0.657 (95% CI: 0.553–0.761), and 0.647 (95% CI: 0.533–0.749), respectively. The optimal eosinophil threshold was 0.035 $\times 10^9$/L, corresponding to a sensitivity of

71.15% and a specificity of 61.70% using the ROC curve to predict the absence of peritonitis. Lower than the threshold eosinophil values were associated with presence of peritonitis (since we inverted the outcome, for ROC comparability). ROC-derived thresholds for MLR (≥0.653), SIRI (≥7.42), and NLR (≥10.855) were associated with higher classification probability of peritonitis. ROC curves are presented in Fig. 1, and full classification parameters are summarized in Table III.

Table II. Comparison between patients with and without peritonitis

Parameters	Presence of peritonitis		p
	Yes (n=52)	No (n=47)	
Age (years)	36 (26 - 54.75)	25 (20.5 - 35.5)	< 0.001
BMI (kg/m^2)	26.23 (23.44 - 30.31)	22.89 (21.18 - 26.73)	0.008
Alvarado score	8 (7 - 9)	7 (6 - 8)	0.002
CRP (mg/L)	30 (10.05 - 30)	7.83 (2.99 - 19.15)	< 0.001
AST (UI/L)	21 (17 - 26)	18 (16 - 24)	0.581
ALT (UI/L)	21 (13.5 - 28)	19 (12 - 30)	0.814
Total bilirubin (mg/dL)	0.91 (0.61 - 1.51)	0.77 (0.56 - 1.01)	0.078
ALP (UI/L)	68 (56.75 - 81)	60 (53 - 76)	0.329
GGT (UI/L)	21.3 (13.5 - 34.5)	22 (12 - 31)	0.504
LDH	198 (164.5 - 233.5)	170 (139 - 193)	0.376
INR	1.15 (1.05 - 1.23)	1.08 (1.02 - 1.12)	0.016
PT (s)	13 (11.7 - 13.9)	12.2 (11.1 - 12.8)	0.018
Urea (mg/dL)	26 (20.5 - 33.5)	24 (19.5 - 29)	0.112
Creatinine (mg/dL)	0.9 (0.72 - 1)	0.78 (0.63 - 0.9)	0.014
Na	136.5 (134 - 138)	138 (136 - 139)	0.02
K	3.99 (3.64 - 4.25)	4.07 (3.79 - 4.45)	0.157
Glycemia (mg/dL)	103 (95 - 118.5)	98 (89.75 - 111)	0.12
Hemoglobin (g/dL)	14.4 (13.17 - 15.1)	13.9 (12.9 - 15.15)	0.601
Leucocytes ×10^9/L	14.2 (10.95 - 17.8)	13 (10.32 - 16.63)	0.197
Neutrophils ×10^9/L	12.45 (8.75 - 15.21)	10.52 (7.93 - 14.11)	0.132
Lymphocytes ×10^9/L	1.29 (0.89 - 1.86)	1.6 (1.09 - 2.09)	0.041
Monocytes ×10^9/L	0.76 (0.58 - 1.07)	0.66 (0.5 - 0.88)	0.086
Eosinophils ×10^9/L	0.02 (0 - 0.05)	0.05 (0.01 - 0.12)	0.005
Basophils ×10^9/L	0.01 (0.01 - 0.02)	0.02 (0.01 - 0.03)	0.035
Platelets ×10^9/L	248.5 (217 - 278)	253 (212.5 - 282.5)	0.908
RDW-CV (%)	13.2 (12.78 - 13.53)	12.9 (12.45 - 13.5)	0.039
PDW (fL)	16.1 (15.88 - 16.33)	16.15 (15.93 - 16.4)	0.617
NLR	11.39 (5.97 - 15.06)	6.92 (4.65 - 11.06)	0.012
dNLR	5.7 (3.75 - 8.57)	4.11 (2.94 - 6.38)	0.053
PLR	190.02 (140.59 - 272.88)	151.8 (120.6 - 231.75)	0.077
MLR	0.71 (0.41 - 0.94)	0.43 (0.29 - 0.63)	0.002
NPR	0.05 (0.04 - 0.06)	0.04 (0.03 - 0.06)	0.048
SII	2267.36 (1438.5 - 4194.22)	1688.21 (1116 - 3154.01)	0.051
SIRI	9.65 (4.07 - 14.19)	5.13 (2.43 - 9.15)	0.007
AISI	2084.4 (916.31 - 3680.35)	1289.94 (511.35 - 2274.9)	0.021

All characteristics are presented as medians (quartile 1 – quartile 3): BMI: body mass index; CRP: C-reactive protein; AST: aspartate aminotransferase; ALT: alanine aminotransferase; ALP: alkaline phosphatase; GGT: gamma-glutamyl transferase; LDH: lactate dehydrogenase; INR: international normalized ratio; PT: prothrombin time; Na: sodium; K: potassium; RDW-CV: red cell distribution width – coefficient of variation; PDW: platelet distribution width; NLR: neutrophil-to-lymphocyte ratio; dNLR: derived neutrophil-to-lymphocyte ratio; PLR: platelet-to-lymphocyte ratio; MLR: monocyte-to-lymphocyte ratio; NPR: neutrophil-to-platelet ratio; SII: systemic immune-inflammation index; SIRI: systemic inflammation response index; AISI: aggregate index of systemic inflammation.

Table III. Classification accuracy of peritonitis with laboratory and inflammatory parameters using receiver operator characteristics

Variable	AUC (95% CI)	p	Sensitivity	Specificity	Cut-off
CRP (mg/L)	0.713 (0.613 - 0.813)	<0.001	70.59	70	15.1
MLR	0.68 (0.577 - 0.784)	0.001	57.69	78.72	0.653
Eosinophils ×10^9/L#	0.663 (0.557 - 0.767)	0.002	71.15	61.7	0.035
SIRI	0.657 (0.553 - 0.761)	0.003	59.62	68.09	7.42
NLR	0.647 (0.533 - 0.749)	0.008	55.77	74.47	10.855
AISI	0.635 (0.531 - 0.741)	0.012	46.15	76.6	2334.554
RDW-CV (%)	0.62 (0.509 - 0.726)	0.03	63.46	59.57	12.95
Lymphocytes ×10^9/L#	0.62 (0.508 - 0.726)	0.031	67.31	55.32	1.52
Basophils ×10^9/L#	0.618 (0.513 - 0.722)	0.027	63.46	57.45	0.015
NPR	0.616 (0.5 - 0.722)	0.051	53.85	70.21	0.052
SII	0.614 (0.5 - 0.722)	0.054	71.15	53.19	1693.879
dNLR	0.613 (0.5 - 0.724)	0.058	65.38	59.57	4.672
PLR	0.604 (0.493 - 0.71)	0.060	65.38	57.45	168.627
Monocytes ×10^9/L	0.6 (0.495 - 0.712)	0.071	63.46	55.32	0.675
Neutrophils ×10^9/L	0.588 (0.473 - 0.7)	0.129	44.23	74.47	13.955
Leucocytes ×10^9/L	0.575 (0.453 - 0.684)	0.203	38.46	76.6	16.665
PDW (fL)#	0.529 (0.414 - 0.64)	0.615	48.08	63.04	16.05
Platelets ×10^9/L#	0.507 (0.389 - 0.621)	0.906	65.38	44.68	259.5

AUC: area under the curve; CI: confidence interval; #, the classification was inverted, so that higher values predict the absence of peritonitis and lower values predict the presence of peritonitis. For the rest of abbreviations see Table II.

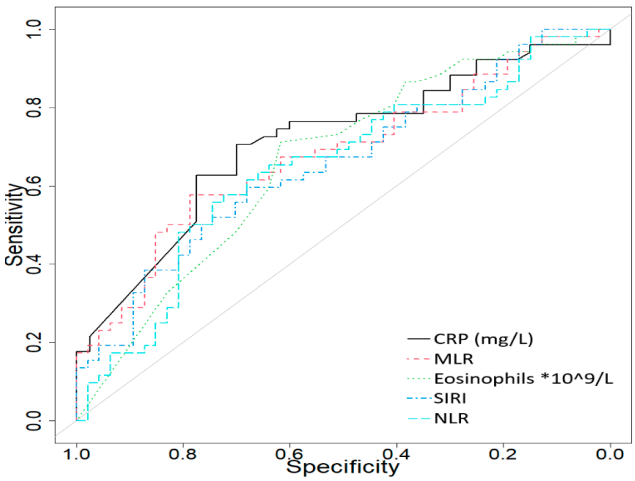

Fig. 1. Receiver operator characteristic predicting peritonitis for different biomarkers.

To evaluate the independent associations, multivariate logistic regression models were constructed based on biomarkers with the highest AUCs, using the identified optimal cut-off values and adjusting for age, sex, time from symptom onset to surgical intervention (<12 h vs. ≥12 h), and Alvarado score.

MLR ≥0.653 remained independently associated with peritonitis [adjusted OR (aOR)=6.92, 95%CI: 2.55–21.21; p<0.001], followed by SIRI ≥7.42 (aOR=6.89, 95%CI: 2.46–22.29; p<0.001) and NLR ≥10.855 (aOR=5.88, 95%CI: 2.16–18.13; p<0.001). In contrast, eosinophil count ≥ 0.035 $\times 10^9$/L was independently associated with lower odds of peritonitis (aOR=0.22, 95%CI: 0.08–0.54; p=0.001). Regression model outcomes are presented in Table IV.

Overall, systemic inflammatory indices, particularly MLR, SIRI, and NLR, demonstrated moderate discriminative ability for identifying peritonitis and remained significantly associated with peritonitis after adjustment for clinically relevant covariates, while higher eosinophil counts were inversely associated with peritonitis.

Table IV. Multivariate logistic regression models using the identified cutoffs, adjusted for age, sex, time from symptom onset to surgical intervention (<12 h vs. ≥12 h), and Alvarado score

Characteristic	OR adjusted	(95% CI)	p
MLR ≥ 0.653	6.92	(2.55 - 21.21)	< 0.001
Eosinophils.10.9/L ≥ 0.035	0.22	(0.08 - 0.54)	0.001
SIRI ≥ 7.42	6.89	(2.46 - 22.29)	< 0.001
NLR ≥ 10.855	5.88	(2.16 - 18.13)	< 0.001

For abbreviations see Tables II and III.

DISCUSSION

The present study shows that, in patients presenting with acute appendicitis and undergoing surgery, the presence of peritonitis is associated with older age, higher BMI, higher Alvarado score and a more pronounced systemic inflammatory response. Among routine laboratory tests, CRP had the highest discriminative ability for peritonitis (AUC=0.71), while several composite blood-cell–derived indices, particularly MLR, SIRI and NLR, also demonstrated moderate discrimination. In

multivariable models adjusted for age, sex, time until surgical intervention, and Alvarado score, MLR ≥0.653, SIRI ≥7.42 and NLR ≥10.855, were independently associated with peritonitis, whereas higher eosinophil counts were inversely associated with peritonitis.

These results are consistent with previous literature on inflammatory biomarkers in acute appendicitis. For example, studies in adult cohorts have demonstrated that NLR is elevated in complicated appendicitis and has diagnostic value [6, 10, 11]. In these studies, composite indices like SIRI and SII have also been shown to distinguish complicated from uncomplicated disease [10-14]. Our findings align with this, while focusing specifically on peritonitis as the complication of interest, which may partly account for the higher thresholds observed for NLR and other ratios. The independent associations of MLR and SIRI in our adjusted models suggests these markers may capture aspects of systemic inflammatory burden and immune cell redistribution that are not fully captured by CRP or simple leukocyte counts [6, 13].

Although our study focused on adults, similar associations between systemic inflammatory indices and disease severity have also been reported in pediatric populations [8, 16-18]. Previous studies have demonstrated that elevated NLR is associated with complicated or perforated appendicitis in children and may serve as an early marker of peritonitis [16-18]. However, pediatric patients often present differently, with faster progression and less specific clinical findings, which may influence biomarker thresholds. Therefore, while the consistency of results suggests a shared pathophysiological mechanism, age-specific validation is needed before extrapolation of cut-off values between adults and children.

The real-world value of markers like MLR and SIRI lies in risk stratification. As our multivariate analysis found (Table IV), patients exceeding the cut-offs had between six to seven-fold increase in the odds of peritonitis (adjusted OR). This suggests they function best as powerful adjuncts to clinical assessment (when combined with standard scoring systems) that can heighten a surgeon suspicion to intervene, rather than as replacement diagnostic tools.

In this context, a potential future application would be the incorporation of hemogram-derived ratios into existing clinical scoring systems for appendicitis, with defined cutoff values to refine risk stratification. Such integration could improve diagnostic accuracy, reduce unnecessary imaging or negative appendectomies, and optimize resource allocation in emergency surgical settings.

This study has several limitations. Its retrospective single-center design and moderate sample size may limit generalizability, and causality cannot be inferred. Additionally, although multivariable adjustment was performed, residual confounding cannot be excluded. Biomarker dynamics over time were not evaluated, and no external validation cohort was available to confirm the proposed cut-offs. Despite these limitations, strengths include a homogeneous cohort of surgically confirmed appendicitis, detailed intraoperative assessment of peritonitis, and comprehensive evaluation of multiple systemic inflammatory indices in comparison with conventional markers.

Importantly, although our study design does not allow for establishing causality, the strength of the associations observed (particularly for MLR, SIRI and NLR, together with low eosinophil counts) suggests that these indices may be valuable in the early recognition of patients at increased risk of presenting with peritonitis. Given that these biomarkers are inexpensive, rapidly obtainable and widely available, they could be incorporated into preoperative assessment to support risk stratification, especially in cases with uncertain clinical presentation or delayed imaging. Future prospective multicenter studies are warranted to validate their performance and to explore whether their integration into decision-making algorithms may improve outcomes by facilitating earlier intervention or closer perioperative monitoring.

CONCLUSIONS

Systemic inflammatory indices higher MLR, SIRI, and NLR values and lower eosinophil counts were significantly associated with intraoperatively confirmed peritonitis in acute appendicitis and remained independently associated after adjustment for clinically relevant covariates. Among the evaluated markers, CRP showed moderate diagnostic performance. Given their low cost and immediate availability, these biomarkers may complement existing diagnostic tools and support earlier preoperative risk stratification for peritonitis, especially when clinical presentation is equivocal or imaging is delayed. Future prospective multicenter studies are required to validate optimal thresholds, evaluate integration into clinical decision-making algorithms, and determine whether biomarker-guided intervention strategies can improve outcomes in acute appendicitis.

Conflicts of interest: None to declare.

Authors' contributions: F.V.M., S.L.P., and D.I.D. conceived the study. F.V.M., V.D.B., and D.C.L. designed the methodology. D.C.L. performed the statistical analysis. F.V.M., R.C., B.S., O.A., and C.B were responsible for patients' management. T.A.D. and S.L.P. collected the data. F.V.M. and V.D.B. drafted the manuscript. D.I.D., S.L.P., and T.A.D. revised the manuscript. D.I.D. supervised the manuscript. All authors have read and agreed to the published version of the manuscript.

REFERENCES

1. Krzyzak M, Mulrooney SM. Acute appendicitis review: background, epidemiology, diagnosis, and treatment. Cureus. 2020;12:e8562. doi:10.7759/cureus.8562
2. Frountzas M, Stergios K, Kopsini D, et al. Alvarado or RIPASA score for diagnosis of acute appendicitis? A meta-analysis of randomized trials. Int J Surg. 2018;56:307–314. doi:10.1016/j.ijsu.2018.07.003
3. Bom WJ, Scheijmans JC, Salminen P, et al. Diagnosis of uncomplicated and complicated appendicitis in adults. Scand J Surg. 2021;110:170–179. doi:10.1177/14574969211008330
4. Bhangu A, Søreide K, Di Saverio S, et al. Acute appendicitis: modern understanding of pathogenesis, diagnosis, and management. Lancet. 2015;386:1278–1287. doi:10.1016/S0140-6736(15)00275-5

5. Hajibandeh S, Hajibandeh S, Hobbs N, et al. Neutrophil-to-lymphocyte ratio predicts acute appendicitis and distinguishes between complicated and uncomplicated appendicitis: a systematic review and meta-analysis. Am J Surg. 2020;219:154–163. doi:10.1016/j.amjsurg.2019.04.018
6. Anastasakis M, Trevlias I, Farmakis K, et al. The importance of the neutrophil–lymphocyte ratio (NLR) and platelet–lymphocyte ratio (PLR) as biomarkers for differentiating complicated and uncomplicated appendicitis. Diagnostics (Basel). 2024;14:2777. doi:10.3390/diagnostics14242777
7. Eun S, Ho IG, Bae GE, et al. Neutrophil-to-lymphocyte ratio for the diagnosis of pediatric acute appendicitis: a systematic review and meta-analysis. Eur Rev Med Pharmacol Sci. 2021;25:7097–7107. doi:10.26355/eurrev_202111_27263
8. Nissen M, Tröbs RB. The lymphocyte-to-monocyte ratio may distinguish complicated from non-complicated pediatric appendicitis: a retrospective study and literature review. Pediatr Neonatol. 2022;63:146–153. doi:10.1016/j.pedneo.2021.08.018
9. Vandenbroucke JP, von Elm E, Altman DG, et al.; STROBE Initiative. Strengthening the reporting of observational studies in epidemiology (STROBE): explanation and elaboration. PLoS Med. 2007;4:e297. doi:10.1371/journal.pmed.0040297
10. Telafarlı MA, Yeni M. The diagnostic value of the systemic immune-inflammatory index in acute appendicitis cases in the emergency department. Langenbecks Arch Surg. 2023;408:136. doi:10.1007/s00423-023-02871-y
11. Saridas A, Vural N, Duyan M, et al. Comparison of the ability of newly inflammatory markers to predict complicated appendicitis. Open Med (Wars). 2024;19:20241002. doi:10.1515/med-2024-1002
12. Berhuni MS, Yönder H, Elkan H, et al. Diagnostic value of systemic immune inflammation index in identifying complicated acute appendicitis cases. Cureus. 2024;16:e73046. doi:10.7759/cureus.73046
13. Hernández-González LL, Serrano-Guzmán SJ, Guzmán-Ortiz JD, et al. C-reactive protein, international normalized ratio, and fibrinogen in diagnostic scale of complicated acute appendicitis. Clin Pract (Basel). 2025;15:25. doi:10.3390/clinpract15020025
14. Halaseh SA, Kostalas M, Kopec CA, et al. Single-center retrospective analysis of neutrophil, monocyte, and platelet-to-lymphocyte ratios as predictors of complicated appendicitis. Cureus. 2022;14:e29177. doi:10.7759/cureus.29177
15. Duyan M, Vural N. Assessment of the diagnostic value of novel biomarkers in adult patients with acute appendicitis: a cross-sectional study. Cureus. 2022;14:e32307. doi:10.7759/cureus.32307
16. Siki FÖ, Sarıkaya M, Gunduz M, et al. Evaluation of the systemic immune inflammation index and the systemic inflammatory response index as new markers for the diagnosis of acute appendicitis in children. Ann Saudi Med. 2023;43:329–338. doi:10.5144/0256-4947.2023.329
17. Bălănescu L, Băetu AE, Cardoneanu AM, et al. Predictors of complicated appendicitis with evolution to appendicular peritonitis in pediatric patients. Medicina (Kaunas). 2023;59:21. doi:10.3390/medicina59010021
18. Tekeli A, Çalışkan MB, Bahadır GB, et al. Evaluation of systemic immune-inflammation index efficacy in predicting complicated appendicitis in pediatric emergency department. Ulus Travma Acil Cerrahi Derg. 2023;29:566–573. doi:10.14744/tjtes.2022.42472