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Predictive Value of Immature Granulocyte Count and C-Reactive Protein For Complicated Acute Appendicitis

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ABSTRACT

Preoperative identification of complicated acute appendicitis is important for surgical planning and perioperative management. This study assessed the associations of preoperative immature granulocyte count (IG#), immature granulocyte percentage (IG%), and C-reactive protein (CRP) with complicated appendicitis and their ability to discriminate complicated from uncomplicated disease.

This retrospective cohort study included 100 adults who underwent appendectomy for acute appendicitis between January and December 2025. Patients were classified as having complicated appendicitis (n=22) or uncomplicated appendicitis (n=78) according to operative and histopathological findings. Group comparisons, receiver operating characteristic (ROC) curve analyses, and a parsimonious multivariable logistic regression model including IG#, CRP, age, and sex were performed.

CRP [58.6 (19.3–155.6) vs. 27.0 (5.3–66.3) mg/L; p = 0.048] and IG# [0.07 (0.06–0.09) vs. 0.06 (0.04–0.08) $\times 10^3/\mu L$; p = 0.039] were higher in complicated appendicitis, whereas IG% did not differ significantly (p = 0.209). The areas under the curve were 0.644 (95% confidence interval [CI]: 0.510–0.779) for IG#, 0.639 (95% CI: 0.505–0.773) for CRP, and 0.587 (95% CI: 0.445–0.729) for IG%. After adjustment, CRP remained independently associated with complicated appendicitis (odds ratio [OR]: 1.122 per 10 mg/L increase; 95% CI: 1.038–1.213; p = 0.004), whereas IG# did not (OR: 1.024 per 0.01 $\times 10^3/\mu L$ increase; 95% CI: 0.970–1.081; p = 0.389).

Among the evaluated biomarkers, only CRP remained independently associated with complicated appendicitis after adjustment. IG# and CRP showed limited discriminatory performance and may be more suitable for clinical risk stratification alongside clinical and imaging findings than for definitive diagnosis in isolation.

Keywords: Acute appendicitis, complicated appendicitis, immature granulocyte count, C-reactive protein, biomarkers

Introduction

Acute appendicitis is one of the most common causes of acute abdominal pain requiring emergency surgical intervention, with an estimated lifetime risk of approximately 7–9% (1–3). Although the diagnosis is often straightforward in patients with typical clinical findings, differentiating uncomplicated from complicated appendicitis before surgery remains a clinically important challenge. Complicated appendicitis, which may include perforation, gangrene, periappendiceal abscess, or phlegmon/plastron formation, is associated with increased morbidity, longer hospitalization, greater need for drainage or open surgical intervention, and more complex postoperative management (1–5). Therefore, early identification of patients at risk for complicated disease may help guide surgical planning and perioperative decision-making.

In current clinical practice, the diagnosis and severity assessment of acute appendicitis are based on a combination of history, physical examination, laboratory parameters, clinical scoring systems, and imaging findings (1–5). Computed tomography and ultrasonography play important roles in the diagnostic work-up; however, imaging may not always clearly distinguish disease severity, and access, cost, radiation exposure, and operator dependence remain relevant considerations in daily practice (2,3). Conventional inflammatory markers such as white blood cell count, neutrophil count, neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio, and C-reactive protein are widely used as supportive tools, but their diagnostic performance in distinguishing complicated from uncomplicated appendicitis has been variable across studies (1,3–6). For this reason, routinely available and inexpensive laboratory parameters that may complement clinical and radiological evaluation continue to attract interest.

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Immature granulocytes are early granulocytic precursors released into the peripheral circulation during systemic inflammation and bone marrow activation. With the use of modern automated hematology analyzers, immature granulocyte count (IG#) and immature granulocyte percentage (IG%) can be obtained as part of a routine complete blood count without additional cost or additional blood sampling (6–14). Previous studies have suggested that immature granulocyte parameters may be associated with infectious and inflammatory disease severity, including acute appendicitis and complicated or perforated appendicitis (6–14). Nevertheless, reported cutoff values and diagnostic performance have not been consistent, and the relative usefulness of IG# compared with IG% remains uncertain.

C-reactive protein is another commonly used marker of systemic inflammation and tissue injury. Elevated CRP levels have been associated with complicated appendicitis in several studies; however, CRP alone may have limited sensitivity or specificity depending on symptom duration, patient characteristics, and the definition of complicated disease (4–6). Therefore, CRP and immature granulocyte parameters should be interpreted as supportive biomarkers rather than standalone diagnostic tests. Their potential clinical value may be greatest when they are evaluated together with clinical assessment and imaging findings.

The present study aimed to evaluate the association of preoperative IG#, IG%, and CRP levels with complicated acute appendicitis in adult patients undergoing appendectomy. A secondary aim was to assess the discriminatory performance of these routinely available biomarkers for distinguishing complicated from uncomplicated appendicitis.

Materials and Methods

Study Design and Ethical Approval: This retrospective cohort study was conducted using the medical records of adult patients who presented to the General Surgery Clinic or Emergency Department of Gaziantep City Hospital with suspected acute appendicitis and subsequently underwent appendectomy. The study was performed in accordance with the principles of the Declaration of Helsinki and the Turkish Personal Data Protection Law. Ethical approval was obtained from the Gaziantep City Hospital Non-Interventional Clinical Research Ethics Committee (Decision No: 417/2026, Date: 21 January 2026).

Patient Selection and Classification: Patients aged 18 years and older who underwent emergency appendectomy for suspected acute appendicitis between January 1, 2025, and December 31, 2025, were retrospectively screened. A total of 102 patients were initially evaluated. After the exclusion of two patients who met the exclusion criteria, the final study cohort consisted of 100 patients.

The diagnosis of acute appendicitis was based on the combined assessment of clinical findings, laboratory parameters obtained at the first emergency department admission, and abdominal imaging findings using computed tomography (CT) and/or ultrasonography (US).

Patients were classified as having complicated or uncomplicated appendicitis according to operative and histopathological findings. Complicated appendicitis was defined by the presence of at least one of the following findings: perforation, gangrene, periappendiceal abscess, phlegmon, or plastron formation documented intraoperatively and/or histopathologically. Patients without any of these findings were classified as having uncomplicated appendicitis. When operative and histopathological findings were discordant, documentation of any qualifying complicated feature in either source resulted in classification as complicated appendicitis.

Inclusion and Exclusion Criteria: The inclusion criteria were as follows: age ≥18 years, emergency appendectomy performed for suspected acute appendicitis, postoperative histopathological confirmation of acute appendicitis, and availability of preoperative laboratory data obtained at the first emergency department admission.

Patients were excluded if they were younger than 18 years, had a histopathological diagnosis of a normal appendix or lymphoid hyperplasia, had hematological disease, active malignancy, chronic inflammatory or autoimmune disease, were receiving immunosuppressive therapy, were pregnant, had evidence of another active infection, or had received antibiotic treatment before admission. During the formation of the final cohort, patient records were screened for all exclusion criteria, and patients meeting any of these criteria were excluded from the analysis.

Data Collection and Laboratory Parameters: Demographic characteristics, including age and sex, clinical findings, symptom duration, body temperature, operative data, surgical approach, operation duration, drain use, imaging findings, and histopathological findings were retrospectively recorded from the hospital information management system.

Imaging findings obtained at the first emergency department admission were reviewed. The recorded imaging parameters included appendiceal diameter, periappendiceal fluid, periappendiceal abscess, phlegmon/plastron formation, and radiological findings suggestive of perforation.

All laboratory values were obtained from venous blood samples collected at the initial emergency department admission before surgical intervention or medical treatment. The analyzed laboratory parameters included white blood cell count, hemoglobin, neutrophil count, lymphocyte count, platelet count, immature granulocyte count (IG#), immature granulocyte percentage (IG%), C-reactive protein (CRP), lactate dehydrogenase, albumin, and creatinine. White blood cell, neutrophil, lymphocyte, platelet, and IG# values were recorded as $\times 10^3/\mu L$. IG% was recorded as percentage, CRP as mg/L, hemoglobin as g/dL, albumin as g/L, lactate dehydrogenase as U/L, and creatinine as mg/dL.

IG# represented the absolute number of immature granulocytes in peripheral blood, whereas IG% represented the proportion of immature granulocytes among total leukocytes. Both parameters were routinely reported as part of the complete blood count analysis using automated hematology analyzers.

Surgical Procedure: All patients underwent emergency appendectomy after the diagnosis of acute appendicitis was established on the basis of clinical, laboratory, and imaging findings. The surgical approach was selected according to the patient's clinical condition and intraoperative findings, and appendectomy was performed using either a laparoscopic or open technique (15,16). A standard multi-port technique was used for laparoscopic appendectomy (16). Abdominal drainage was used selectively in patients with complicated appendicitis, particularly in the presence of perforation, intra-abdominal contamination, or periappendiceal collection (17). Perioperative antibiotic prophylaxis was administered to all patients in accordance with institutional practice and current surgical recommendations (15,16). Surgical approach, operative duration, and drain use were recorded for analysis.

Statistical Analysis: Primary statistical analyses were performed using IBM SPSS Statistics for Windows, Version 26.0 (IBM Corp., Armonk, NY, USA). The normality of continuous variables was assessed using visual methods, including histograms and Q–Q plots, and analytical tests, including the Kolmogorov–Smirnov and Shapiro–Wilk tests. Continuous variables that were not normally distributed were presented as median and interquartile range (IQR), whereas categorical variables were expressed as numbers and percentages. The Mann–Whitney U test was used to compare continuous variables between the complicated and uncomplicated appendicitis groups. Categorical variables were compared using the chi-square test or Fisher's exact test, as appropriate.

Receiver operating characteristic (ROC) curve analysis was performed to evaluate the ability of IG#, IG%, and CRP to discriminate complicated appendicitis. The area under the curve (AUC) was reported with 95% confidence intervals (CIs). Optimal cutoff values were identified using the Youden index. Sensitivity and specificity at the selected cutoff values were reported with exact binomial 95% CIs calculated using the Clopper–Pearson method. The reporting of diagnostic accuracy-related analyses was guided by the principles of the STARD 2015 statement where applicable (18).

Multivariable logistic regression analysis was performed to evaluate whether IG# and CRP were independently associated with complicated appendicitis. IG# and CRP were included as the biomarkers of primary interest, whereas age and sex were included as basic clinically relevant demographic covariates. Given the limited number of complicated appendicitis events (n=22), the number of covariates was intentionally restricted and a parsimonious model was constructed to reduce the risk of overfitting and unstable effect estimates. Results were reported as odds ratios (ORs) with 95% confidence intervals.

Because of the retrospective design, no a priori power analysis was performed. The sample size was determined by the inclusion of all eligible patients who met the study criteria during the defined study period. A two-sided p-value of <0.05 was considered statistically significant.

Results

A total of 100 adult patients who underwent appendectomy for acute appendicitis were included in the study. According to operative and histopathological findings, 22 patients (22.0%) were classified as having complicated appendicitis and 78 patients (78.0%) as having uncomplicated appendicitis.

The overall cohort consisted of 69 male patients and 31 female patients. Male sex was observed in 12 patients (54.5%) in the complicated appendicitis group and in 57 patients (73.1%) in the uncomplicated appendicitis group, with no statistically significant difference between the groups ($p = 0.162$).

Table 1: Comparison of Continuous Variables Between Patients With Complicated and Uncomplicated Appendicitis

Variable	Complicated appendicitis (n=22), median (IQR)	Uncomplicated appendicitis (n=78), median (IQR)	p-value
Age (years)	27.0 (20.0–43.0)	31.0 (24.3–42.8)	0.389
Symptom duration (hours)	26.0 (24.0–66.0)	36.0 (24.0–48.0)	0.550
Body temperature (°C)	36.5 (36.3–37.0)	36.5 (36.1–36.9)	0.214
Appendix diameter (mm)	9.0 (7.7–11.5)	9.0 (8.0–10.0)	0.601
Hemoglobin (g/dL)	13.5 (12.9–14.1)	14.6 (12.7–15.8)	0.008
WBC count (×10³/μL)	13.4 (10.2–15.9)	12.8 (9.3–15.6)	0.378
Neutrophil count (×10³/μL)	11.0 (7.2–12.8)	9.7 (6.3–13.1)	0.396
Lymphocyte count (×10³/μL)	1.90 (1.37–2.41)	1.95 (1.41–2.64)	0.803
Platelet count (×10³/μL)	292.5 (247.8–373.8)	260.0 (223.5–331.3)	0.156
CRP (mg/L)	58.6 (19.3–155.6)	27.0 (5.3–66.3)	0.048
LDH (U/L)	230.7 (182.8–256.3)	204.4 (181.3–237.3)	0.200
Albumin (g/L)	43.0 (38.7–45.3)	45.1 (40.0–47.4)	0.081
Creatinine (mg/dL)	0.74 (0.59–0.94)	0.82 (0.70–0.91)	0.360
IG# (×10³/μL)	0.07 (0.06–0.09)	0.06 (0.04–0.08)	0.039
IG% (%)	0.55 (0.40–0.70)	0.40 (0.30–0.60)	0.209
Operation duration (min)	48.5 (45.0–63.8)	50.0 (40.0–55.0)	0.235
Length of hospital stay (days)	2.0 (1.0–2.8)	2.0 (1.0–2.8)	0.383

Continuous variables are presented as median and interquartile range. Comparisons between groups were performed using the Mann–Whitney U test. CRP: C-reactive protein; IG#: immature granulocyte count; IG%: immature granulocyte percentage; IQR: interquartile range; LDH: lactate dehydrogenase; WBC: white blood cell count

The comparison of continuous variables between the complicated and uncomplicated appendicitis groups is shown in Table 1. Preoperative CRP levels were significantly higher in patients with complicated appendicitis than in those with uncomplicated appendicitis [58.6 (19.3–155.6) vs. 27.0 (5.3–66.3) mg/L; p = 0.048]. Similarly, IG# values were higher in the complicated appendicitis group [0.07 (0.06–0.09) vs. 0.06 (0.04–0.08) ×10³/μL; p = 0.039]. In contrast, IG% did not differ significantly between the groups [0.55 (0.40–0.70) vs. 0.40 (0.30–0.60)%; p = 0.209].

Among the other continuous laboratory parameters, preoperative hemoglobin levels were significantly lower in patients with complicated appendicitis than in those with uncomplicated appendicitis [13.5 (12.9–14.1) vs. 14.6 (12.7–15.8) g/dL; p = 0.008]. No statistically significant differences were observed between the groups in terms of age, symptom duration, body temperature, appendix diameter, WBC count, neutrophil count, lymphocyte count, platelet count, LDH, albumin, creatinine, operation duration, or length of hospital stay.

The comparison of categorical variables is presented in Table 2. Ultrasonography was performed more frequently in the complicated appendicitis group than in the uncomplicated appendicitis group [7/22 (31.8%) vs. 8/78 (10.3%); p = 0.020]. Computed tomography was performed in all patients; therefore, CT use was not included in between-group

Table 2: Comparison of Categorical Variables Between Patients With Complicated and Uncomplicated Appendicitis

Variable	Complicated appendicitis (n=22), n (%)	Uncomplicated appendicitis (n=78), n (%)	p-value
Male sex	12 (54.5%)	57 (73.1%)	0.162
Ultrasonography performed	7 (31.8%)	8 (10.3%)	0.020
Computed tomography performed	22 (100.0%)	78 (100.0%)	NA
Periappendiceal fluid/abscess	12 (54.5%)	23 (29.5%)	0.042
Open surgical approach	4 (18.2%)	3 (3.8%)	0.040
Drain use	15 (68.2%)	31 (39.7%)	0.028

Categorical variables are presented as numbers and percentages. Comparisons between groups were performed using the chi-square test or Fisher's exact test, as appropriate. Computed tomography was performed in all patients; therefore, between-group statistical comparison was not applicable for this variable. NA: not applicable

Table 3: ROC Analysis of IG#, CRP, and IG% For Predicting Complicated Appendicitis

Parameter	AUC (95% CI)	Optimal cutoff value	Sensitivity, % (95% CI)	Specificity, % (95% CI)
IG#	0.644 (0.510–0.779)	≥0.06 $\times 10^3/\mu L$	77.3 (54.6–92.2)	48.7 (37.2–60.3)
CRP	0.639 (0.505–0.773)	≥119.74 mg/L	36.4 (17.2–59.3)	88.5 (79.2–94.6)
IG%	0.587 (0.445–0.729)	≥0.60%	50.0 (28.2–71.8)	71.8 (60.5–81.4)

AUC: area under the curve; CI: confidence interval; CRP: C-reactive protein; IG#: immature granulocyte count; IG%: immature granulocyte percentage; ROC: receiver operating characteristic. Optimal cutoff values were determined using the Youden index. The 95% CIs for sensitivity and specificity were calculated using the exact Clopper–Pearson method

Table 4: Multivariable Logistic Regression Analysis For Complicated Appendicitis

Variable	OR	95% CI	p-value
IG#, per 0.01 $\times 10^3/\mu L$ increase	1.024	0.970–1.081	0.389
CRP, per 10 mg/L increase	1.122	1.038–1.213	0.004
Age, per 1-year increase	0.956	0.914–1.000	0.051
Male sex	0.258	0.083–0.806	0.020

CI: confidence interval; CRP: C-reactive protein; IG#: immature granulocyte count; OR: odds ratio. The model was adjusted for IG#, CRP, age, and sex. CRP was entered per 10 mg/L increase, and IG# was entered per 0.01 $\times 10^3/\mu L$ increase

significance testing. Periappendiceal fluid or abscess was more frequently observed in patients with complicated appendicitis [12/22 (54.5%) vs. 23/78 (29.5%); p = 0.042]. The rate of open surgical approach was higher in the complicated appendicitis group [4/22 (18.2%) vs. 3/78 (3.8%); p = 0.040]. Drain use was also more common in patients with complicated appendicitis [15/22 (68.2%) vs. 31/78 (39.7%); p = 0.028].

Receiver operating characteristic curve analysis was performed to evaluate the discriminatory performance of IG#, CRP, and IG% for complicated appendicitis. All three biomarkers demonstrated limited discriminatory performance. IG# had an AUC of 0.644 (95% CI: 0.510–0.779). At the optimal cutoff value of ≥0.06 $\times 10^3/\mu L$, its sensitivity was 77.3% (95% CI: 54.6–92.2) and its specificity was 48.7% (95% CI: 37.2–60.3). CRP had an AUC of 0.639 (95% CI: 0.505–0.773). At the optimal cutoff value of ≥119.74 mg/L, its sensitivity was 36.4% (95% CI: 17.2–59.3) and its specificity was 88.5% (95% CI: 79.2–94.6). IG% had an AUC of 0.587 (95% CI:

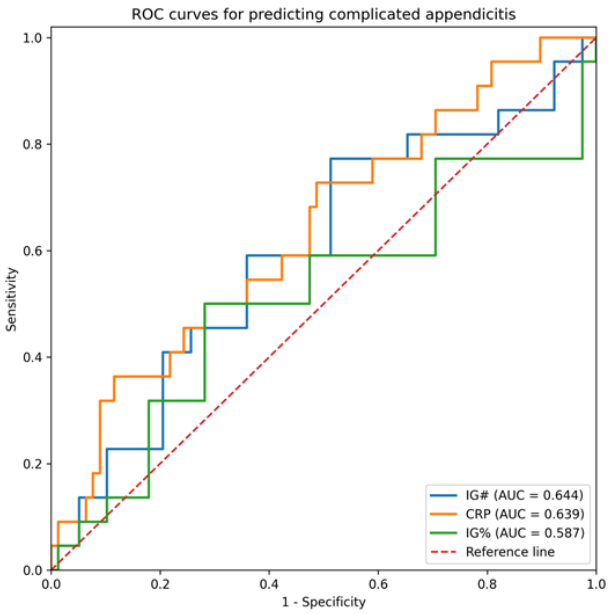

Fig. 1. ROC curves of IG#, CRP, and IG% for predicting complicated appendicitis

0.445–0.729). At the optimal cutoff value of ≥0.60%, its sensitivity was 50.0% (95% CI: 28.2–71.8) and its specificity was 71.8% (95% CI: 60.5–81.4) (Figure 1 and Table 3).

Optimal cutoff values were determined using the Youden index. The 95% CIs for sensitivity and specificity were calculated using the exact Clopper–Pearson method.

A parsimonious multivariable logistic regression model was constructed to evaluate whether IG# and CRP were independently associated with complicated appendicitis after adjustment for age and sex. CRP remained independently associated with complicated appendicitis (OR: 1.122 per 10 mg/L increase; 95% CI: 1.038–1.213; p = 0.004), whereas IG# was not independently associated with the outcome (OR: 1.024 per 0.01 $\times 10^3/\mu L$ increase; 95% CI: 0.970–1.081; p = 0.389). Male sex was inversely associated with complicated appendicitis in the adjusted model (OR: 0.258; 95% CI: 0.083–0.806; p = 0.020), whereas age did not reach statistical significance (OR: 0.956 per 1-year increase; 95% CI: 0.914–1.000; p = 0.051). Given the limited number of complicated appendicitis events, all adjusted findings should be interpreted cautiously (Table 4).

Discussion

In the present study, preoperative CRP and IG# levels were significantly higher in patients with complicated appendicitis than in those with uncomplicated appendicitis, whereas IG% did not differ significantly between the groups. ROC analysis showed that IG#, CRP, and IG% had only limited discriminatory performance for predicting complicated appendicitis. In the multivariable logistic regression model adjusted for age and sex, CRP remained independently associated with complicated appendicitis, while IG# showed a positive but non-significant association. These findings suggest that preoperative CRP and IG# may provide supportive information in the assessment of complicated appendicitis, but they should not be interpreted as standalone diagnostic markers.

An additional finding of the adjusted analysis was the inverse association between male sex and complicated appendicitis. Importantly, sex was not significantly associated with complicated appendicitis in the unadjusted comparison, and this finding was not a primary objective of the study. Given the small number of complicated appendicitis events and the intentionally restricted multivariable model, this association may reflect sample-specific variation, residual confounding, or model instability. Therefore, it should be interpreted cautiously and should not be considered evidence of a protective effect of male sex. Confirmation in larger prospective cohorts is required.

Distinguishing complicated from uncomplicated appendicitis before surgery remains clinically important because complicated disease may affect surgical strategy, need for drainage, antibiotic planning, and postoperative follow-up (1–5). In daily practice, this distinction is usually based on a combination of clinical evaluation, laboratory parameters, scoring systems, and imaging findings. Although CT and US are widely used in the diagnostic work-up, laboratory biomarkers remain attractive because they are inexpensive, rapidly available, and easily repeatable. However, no single laboratory parameter has sufficient diagnostic accuracy to replace clinical assessment or imaging. Therefore, biomarkers such as CRP, WBC count, neutrophil count, neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and IG parameters should be considered complementary tools rather than definitive diagnostic tests (1,3–6).

The role of immature granulocytes in acute appendicitis has attracted increasing attention in recent years. Immature granulocytes reflect bone marrow activation and the release of early granulocytic precursors into peripheral blood during systemic inflammation. Turkes et al. reported that both immature granulocyte count and percentage were significantly higher in patients with complicated appendicitis (7). Similarly, Güler et al. suggested that immature granulocyte parameters may be useful in

patients with suspected acute appendicitis, particularly when interpreted together with clinical assessment (9). In contrast, Altunok and Altınsoy reported that IG% had limited discriminatory value in acute appendicitis (8). The findings of the present study are consistent with this heterogeneous literature. IG# was significantly higher in complicated appendicitis in univariate analysis, whereas IG% was not significantly different between the groups.

The difference between IG# and IG% may be clinically relevant. IG# represents the absolute number of immature granulocytes in peripheral blood, whereas IG% reflects their proportion within the total leukocyte count. In acute inflammatory conditions, changes in total leukocyte count may influence the relative percentage of immature granulocytes and may partly explain the weaker performance of IG%. In our study, IG# showed a higher AUC than IG%, although its overall discriminatory ability remained limited. Moreover, IG# did not remain independently associated with complicated appendicitis after adjustment for age, sex, and CRP. This suggests that IG# may reflect inflammatory burden but may not provide sufficient independent predictive information when evaluated together with CRP and basic clinical variables.

More recently, Cumaoglu et al. evaluated several inflammatory and immune-nutritional markers, including delta neutrophil index, CRP/albumin ratio, procalcitonin, immature granulocytes, and HALP score, and emphasized that combined biomarker models may provide more clinically useful information than isolated parameters (19). Similarly, regression-based analyses in elderly patients with acute appendicitis have suggested that laboratory parameters may contribute to risk stratification and prediction of adverse clinical outcomes (20).

CRP is one of the most widely used inflammatory biomarkers in acute appendicitis. Several studies have reported that elevated CRP levels are associated with complicated or perforated appendicitis (4–6,21). In the present study, CRP levels were significantly higher in the complicated appendicitis group, and CRP remained independently associated with complicated appendicitis in the adjusted logistic regression model. However, the ROC analysis showed that the discriminatory performance of CRP was also limited. The CRP cutoff value of ≥119.74 mg/L demonstrated relatively high specificity but low sensitivity. This means that markedly elevated CRP may increase the likelihood of complicated appendicitis, but a lower CRP value cannot reliably exclude complicated disease.

The diagnostic performance of IG# and CRP in this study should therefore be interpreted cautiously. The AUC values of IG# and CRP were close to 0.64, indicating modest discrimination rather than strong diagnostic accuracy. IG# showed relatively higher sensitivity but lower specificity, whereas CRP showed higher specificity but lower sensitivity. From a clinical perspective, this pattern suggests that IG# may be more useful as an early supportive marker, while markedly elevated CRP may be more suggestive of complicated inflammation. Accordingly, neither parameter is sufficiently accurate for definitive diagnosis when used in isolation. Their potential clinical role may be better framed as contributing to risk stratification when integrated with clinical and imaging findings.

Comparison with established inflammatory markers further supports this cautious interpretation. Conventional parameters such as WBC count, neutrophil count, NLR, and PLR are frequently evaluated in patients with acute appendicitis, but their performance in distinguishing complicated from uncomplicated disease varies across studies (1,3–6). In our cohort, WBC, neutrophil, lymphocyte, and platelet counts were not significantly different between the groups. This may reflect the multifactorial nature of complicated appendicitis and the limited ability of individual hematological parameters to capture disease severity. Clinical scoring systems, such as the Alvarado score and other appendicitis risk scores, may improve diagnostic stratification when combined with laboratory and imaging findings; however, these scores were not systematically available in our retrospective dataset. Therefore, the present findings support the use of IG# and CRP as adjunctive biomarkers rather than replacements for structured clinical evaluation.

An additional finding of the current study was that preoperative hemoglobin levels were lower in patients with complicated appendicitis. This result should be interpreted cautiously because hemoglobin was not a primary outcome variable and may be influenced by age, sex, hydration status, comorbidities, and inflammatory burden. Ünal et al. also reported that hemoglobin and albumin-related immune-nutritional indices may be associated with complicated appendicitis (4). However, the clinical relevance of lower hemoglobin in the present cohort remains uncertain and requires further investigation in larger studies.

Radiological and operative findings in our study were consistent with the clinical definition of complicated appendicitis. Periappendiceal fluid or abscess was more common in patients with complicated appendicitis, and these patients more frequently underwent open surgery and drain placement. These findings support the importance of integrating

laboratory biomarkers with imaging and intraoperative assessment. Kang et al. emphasized that combining peripheral blood biomarkers with clinical features may improve the prediction of pathological subtypes of acute appendicitis (2). Similarly, Yazla et al. suggested that laboratory parameters may be more clinically informative when interpreted together with imaging findings and disease severity indicators (5).

Overall, preoperative IG# and CRP levels were higher in patients with complicated appendicitis, but both biomarkers demonstrated limited discriminatory performance. Among the evaluated biomarkers, only CRP remained independently associated with complicated appendicitis after adjustment for age and sex. Accordingly, IG# and CRP should be interpreted as adjunctive laboratory parameters rather than standalone diagnostic tests. Larger prospective studies incorporating clinical scores, imaging findings, and combined biomarker models are needed to better define their role in the preoperative assessment of complicated acute appendicitis.

Limitations: This study has several limitations that should be considered when interpreting the findings. First, the retrospective and single-center design may limit the generalizability of the results and may introduce selection bias. Second, the total sample size was relatively limited, and the number of patients with complicated appendicitis was small. This may have reduced the statistical power of the study and may have affected the reliability of ROC-derived cutoff values.

Third, because of the retrospective design, no a priori power analysis was performed. Instead, all eligible patients who met the inclusion criteria during the predefined study period were included. Therefore, the findings should be interpreted as exploratory and should be validated in larger prospective cohorts. Fourth, although multivariable logistic regression analysis was performed, the limited number of complicated appendicitis events required the use of a parsimonious model. As a result, only a small number of clinically relevant variables could be included to reduce the risk of overfitting. This limitation may have influenced the assessment of the independent predictive value of IG# and CRP.

Fifth, clinical scoring systems such as the Alvarado score or other appendicitis risk scores were not systematically available in the medical records and therefore could not be incorporated into the analysis. Similarly, some inflammatory and prognostic biomarkers, including procalcitonin, CRP/albumin ratio, neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio, and hemoglobin–albumin–lymphocyte–platelet score, were not evaluated as combined predictive models. Sixth, although complicated appendicitis was defined according to operative and histopathological findings, retrospective interpretation of these records may be subject to documentation variability.

Finally, the AUC values of IG#, CRP, and IG% indicated limited discriminatory performance. Therefore, these biomarkers should not be considered standalone diagnostic tools. The results should be interpreted in conjunction with clinical assessment, imaging findings, and intraoperative evaluation. Larger, multicenter, prospective studies are needed to validate these findings and to determine whether combined clinical, radiological, and laboratory models can improve the preoperative prediction of complicated acute appendicitis.

Preoperative CRP and IG# levels were higher in patients with complicated appendicitis than in those with uncomplicated appendicitis; however, both biomarkers demonstrated limited discriminatory performance. Among the evaluated biomarkers, only CRP remained independently associated with complicated appendicitis after adjustment for age and sex, whereas IG# did not.

Accordingly, neither IG# nor CRP should be used as a standalone diagnostic test. These parameters may provide adjunctive information when interpreted together with patient history, physical examination, and imaging findings. Larger multicenter prospective studies are needed to validate these findings and to determine whether combined clinical, radiological, and laboratory models improve the preoperative identification of complicated appendicitis.

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