

# Value of neutrophil-to-platelet ratio, immature granulocyte-to-lymphocyte ratio, red blood cell distribution width-to-lymphocyte ratio in differentiating complicated acute appendicitis

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## ABSTRACT

**BACKGROUND:** The discovery that medical treatment could be successful in cases with uncomplicated acute appendicitis (UCAA) has revealed the need for successfully differentiating cases with complicated acute appendicitis (CAA). The present study examined the usability of neutrophil-to-platelet ratio (NPR), immature granulocyte-to-lymphocyte ratio, and red blood cell distribution width-to-lymphocyte ratio (RDWLR) in the CAA/UCAA differentiation.

**METHODS:** A retrospective evaluation was made of patients undergoing appendectomy between January 2019 and December 2020. According to pathological and clinical findings, the patients were divided into negative appendectomy, CAA and UCAA groups. Laboratory parameters and associated ratios were evaluated by comparing the groups.

**RESULTS:** The study included 348 patients. Of the patients, 11.2% had CAA, 81.6% had UCAA, and 7.2% had negative appendectomy. The neutrophil-to-lymphocyte ratio (AUC=0.742), platelet-to-lymphocyte ratio (AUC=0.707), immature granulocyte-to-lymphocyte ratio (AUC=0.782), monocyte-to-lymphocyte ratio (AUC=0.720), and RDWLR (AUC=0.711) were found significant in the differentiation between complicated and uncomplicated AA. The NPR (AUC=0.789) was found to be significant in the differentiation between positive and negative appendectomy.

**CONCLUSION:** It was concluded that the immature granulocyte-to-lymphocyte ratio, NPR, monocyte-to-lymphocyte, and RDWLR, which have not been previously studied in patients with acute appendicitis (AA), could be used to differentiate between complicated and uncomplicated AA groups.

**Keywords:** Acute appendicitis; complicated appendicitis; Immature granulocyte-to-lymphocyte ratio; monocyte-to-lymphocyte ratio; neutrophil-to-platelet ratio; red blood cell distribution width-to-lymphocyte ratio.

## INTRODUCTION

For more than a century, surgery has been used as the gold standard in the treatment of acute appendicitis (AA), which is one of the most common causes of acute abdomen in the adult patient group.<sup>[1]</sup> In accordance with today's treatment approaches, the usability of non-operative treatment methods in AA patients, whose treatment is primarily surgical to

reduce morbidity, is being evaluated.<sup>[2]</sup> For the general acceptance of this approach, the selection criteria and treatment plans for the patient group should be established more clearly.

Cases with perforation, gangrene, and abscess are classified as complicated AA (CAA).<sup>[3]</sup> The success of conservative treatment in patients with uncomplicated AA (UCAA) cannot be achieved in patients with CAA, and although medical therapy

Cite this article as: Kubat M, Şengül S. Value of neutrophil-to-platelet ratio, immature granulocyte-to-lymphocyte ratio, red blood cell distribution width-to-lymphocyte ratio in differentiating complicated acute appendicitis. *Ulus Travma Acil Cerrahi Derg* 2022;28:607-614.

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*Ulus Travma Acil Cerrahi Derg* 2022;28(5):607-614 DOI: 10.14744/tjtes.2021.30434 Submitted: 08.03.2021 Accepted: 31.08.2021

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is required in some cases such as plastron AA, the likelihood of using surgical methods for treatment in complicated patients is still high.<sup>[4]</sup> Therefore, it becomes a priority to differentiate between uncomplicated and complicated cases before treatment planning. Although it is not considered to be an erroneous treatment choice when patients undergoing appendectomy under the assumption of CAA are postoperatively detected to have UCAA, delay in the treatment of patients who are classified as UCAA but actually have CAA, should be avoided as a result of concern for increased morbidity.<sup>[4]</sup>

Due to the importance of the difference between CAA and UCAA, research has been carried out and is still ongoing into the efficacy of many clinical, laboratory, and radiological parameters in the differentiation.<sup>[5]</sup> Scoring systems developed using patients' clinical, laboratory and radiological findings are also revised and the results are used to differentiate between CAA and UCAA.<sup>[6]</sup> None of these methods with demonstrated efficacy has been sensitive and specific enough to be called the gold standard.

Several studies have evaluated the hematological parameters (mainly leukocyte, neutrophil, and lymphocyte counts) of the complete blood count (CBC) and laboratory findings such as C-reactive protein (CRP), procalcitonin, and total bilirubin (T.BIL), which are commonly used in clinical practice, for the differentiation between CAA and UCAA and most of these parameters have been found to be statistically significant.<sup>[5]</sup> It is believed that CAA and UCAA can be differentiated by laboratory tests on a clinical basis.<sup>[7]</sup> Although results from laboratory tests are effective in differentiating complicated cases, studies show that the indirect results obtained through mathematical ratios, such as the ratio of selected hematological parameters to each other, have higher efficacy.<sup>[8]</sup>

The aim of our study is to evaluate the laboratory results used to diagnose AA and to differentiate between CAA and UCAA, as well as the new indirect parameters obtained using these results, to examine their usability in the differentiation.

## MATERIALS AND METHODS

A retrospective review was made of the medical records of patients aged  $\geq 18$  years who underwent appendectomy with a pre-diagnosis of AA between January 2019 and December 2020 at a tertiary healthcare facility, and did not have any comorbidity. The demographic, clinical, pathological, radiological, and laboratory data retrieved from the hospital registry system were recorded. Among the 363 patients with full records, four patients with primary ovarian pathologies, one patient with Meckel's diverticulum, one patient with Amyand's hernia, one patient with urinary pathology, and one patient with colonic inflammatory pathology were excluded after clinical and pathological examination, and two patients with mucinous adenocarcinoma, two patients with neuroendocrine tumor, two patients with mucocele, and one patient with serrated

adenoma were excluded after pathological examination. The study continued with the remaining 348 patients.

Among the CBC and biochemical parameters, our study utilized leukocytes (white blood cells) (WBC) (range: 4.49–12.68  $10^3/uL$ ), platelets (PLT) (range: 173–390  $10^3/uL$ ), neutrophils (range: 2.1–8.89  $10^3/uL$ ), lymphocytes (range: 1.26–3.35  $10^3/uL$ ), monocytes (range: 0.25–0.84  $10^3/uL$ ), red blood cell distribution width (RDW-CV) (range: 12.1–14.3%), immature granulocytes (IGs) (range: 0.0–0.06  $10^3/uL$ ), CRP (range: 0–0.5 mg/dl), and T.BIL (range: 0.2–1.2 mg/dl) as well as the neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), neutrophil-to-platelet ratio (NPR), immature granulocytes-to-lymphocyte ratio (IGLR), monocyte-to-lymphocyte ratio (MLR), and red blood cell distribution width-to-lymphocyte ratio (RDWLR).

Patients were divided into negative appendectomy (with no appendicitis pathologically) (NA), CAA and UCAA groups according to a post-operative histopathological examination. A positive appendectomy (pathologically diagnosed appendicitis) (PA) group was defined by combining the CAA and UCAA groups.

## Statistical Methods

Mean, standard deviation, median, minimum, maximum value frequency, and percentage were used for descriptive statistics. The distribution of variables was checked with Kolmogorov–Smirnov test. Kruskal–Wallis and Mann–Whitney U tests were used for the comparison of quantitative data. The Chi-square test was used for the comparison of the qualitative data. ROC analysis was used to show the effect level. Logistic regression was used to show the effect level. SPSS 27.0 was used for statistical analyses.

All data collection and analysis were carried out with the approval of local ethics committee (decision date/number 13.01.2021/01-15) Written consent was obtained from the hospital administration and other surgeons who carried out the treatment of the patients.

## RESULTS

Of 348 study patients, 64.4% (n=224) were male and the mean age was 33.36 ( $\pm 13.49$ ) years. CAA was detected in 11.2% (n=39), UCAA in 81.6% (n=284), and NA in 7.2% (n=25) of the patients.

Age, gender distribution, and PLT, and RDW-CV values did not differ significantly between the NA, UCAA, and CAA groups ( $p=0.070$ ,  $p=0.590$ ,  $p=0.331$ ,  $p=0.210$ , and  $p=0.274$ , respectively). When the NA, UCAA, and CAA groups were evaluated together, the WBC, neutrophil, lymphocyte, IG, CRP, NLR, PLR, NPR, IGLR, MLR, and RDWLR values were found to differ significantly ( $p<0.001$  for all) (Table 1).

**Table 1.** Comparison of the data between the negative appendicitis, uncomplicated acute appendicitis, and complicated acute appendicitis groups

	Negative appendectomy		Uncomplicated AA		Complicated AA		p <sup>k</sup>	p <sup>1m</sup>	p <sup>2m</sup>	p <sup>3m</sup>
	Mean±SD/n-%	Median	Mean±SD/n-%	Median	Mean±SD/n-%	Median				
WBC	10.83±2.92	10.71	14.10±4.26	14.03	16.56±4.15	16.05	<0.001	<0.001	<0.001	0.001
PLT	267.64±50.53	269.0	251.96±65.26	247.5	261.87±65.97	248.0	0.210	0.114	0.726	0.327
Neutrophil	7.35±2.89	7.11	10.88±4.02	10.88	13.77±4.25	13.19	<0.001	<0.001	<0.001	<0.001
Lymphocyte	2.52±1.13	2.46	2.14±1.23	2.04	1.56±1.01	1.27	<0.001	0.041	<0.001	<0.001
Monocyte	0.78±0.29	0.74	0.98±0.39	0.94	1.06±0.43	0.95	0.009	0.006	0.002	0.342
RDW-CV	12.58±0.88	12.30	12.90±1.43	12.50	13.22±1.70	12.60	0.274	0.375	0.116	0.215
IG	0.04±0.03	0.03	0.05±0.03	0.05	0.09±0.06	0.08	<0.001	0.006	<0.001	<0.001
CRP	2.68±4.05	0.70	2.98±4.13	1.15	9.32±8.84	8.30	<0.001	0.358	<0.001	<0.001
T.BIL	0.65±0.37	0.60	0.83±0.59	0.67	0.99±0.60	0.84	0.018	0.113	0.009	0.026
NLR	4.15±3.92	2.55	6.49±4.58	5.48	12.11±7.70	11.71	<0.001	<0.001	<0.001	<0.001
PLR	131.45±73.04	111.41	147.44±98.30	122.44	218.07±113.39	213.95	<0.001	0.328	0.001	<0.001
NPR (1/10 <sup>3</sup> )	28.58±13.10	25.16	44.83±17.34	43.97	54.57±17.22	54.044	<0.001	<0.001	<0.001	0.001
IGLR (1/10 <sup>3</sup> )	19.47±17.11	10.70	31.04±24.70	25.52	82.55±74.37	63.063	<0.001	0.002	<0.001	<0.001
MLR	0.412±0.346	0.290	0.544±0.379	0.460	0.847±0.471	0.829	<0.001	0.002	<0.001	<0.001
RDWLR	6.57±4.61	5.00	7.75±5.46	6.41	11.34±5.93	9.764	<0.001	0.031	<0.001	<0.001

<sup>k</sup>Kruskal-wallis test; <sup>m</sup>Mann-Whitney U test/<sup>χ</sup> Chi-square test. <sup>1</sup>Difference Between NA and UCAA; <sup>2</sup>Difference Between NA and CAA; <sup>3</sup>Difference Between UCAA and CAA. AA: Acute appendicitis; WBC: White blood cells; PLT: Platelets; RDW-CV: Red blood cell distribution width; IG: Immature granulocyte; CRP: C-reactive protein; T.BIL: Total bilirubin; NLR: Neutrophil-to-lymphocyte ratio; PLR: Platelet-to-lymphocyte ratio; NPR: Neutrophil-to-platelet ratio; IGLR: IG-to-Lymphocyte ratio; MLR: Monocyte-to-Lymphocyte Ratio; RDWLR: red blood cell distribution width-to-lymphocyte ratio; SD: Standard deviation.

When the CAA group was compared with the UCAA group, the neutrophil, IG, CRP, NLR, PLR, NPR, IGLR, MLR, and RDWLR values ( $p \leq 0.001$  for all) and WBC were ( $p = 0.001$ ) significantly higher. The lymphocyte value was significantly lower ( $p < 0.001$ ). While the CRP value differed significantly between the NA and CAA groups ( $p < 0.001$ ), there was no significant difference between the NA and UCAA groups ( $p = 0.358$ ). Likewise, the PLR and T.BIL values differed significantly between the NA and CAA groups ( $p < 0.001$  and  $p = 0.009$ , respectively), but not significantly between the NA and UCAA groups ( $p = 0.328$  and  $p = 0.113$ , respectively). The monocyte value was significantly higher in the CAA and UCAA groups ( $p = 0.002$  and  $p = 0.006$ ) when compared with the NA group. The monocyte value did not differ significantly ( $p = 0.342$ ) between the CAA and UCAA groups (Table 1).

The univariate model revealed significant efficacy of WBC, neutrophil, monocyte, IG, NLR, NPR, IGLR, MLR, and RDWLR values in differentiating between the NA and PA groups. The multivariate model revealed significant-independent efficacy of NPR ( $p < 0.001$ ) in differentiating between the NA and PA groups (Table 2).

The univariate model revealed significant efficacy of WBC, neutrophil, lymphocyte, IG, NLR, NPR, IGLR, MLR, and RDWLR values in differentiating between the UCAA and CAA groups. The multivariate model revealed significant-indepen-

dent efficacy of CRP ( $p < 0.001$ ), and IGLR ( $p < 0.001$ ) in differentiating between the UCAA and CAA groups (Table 2).

In differentiating between the NA and PA patients, WBC's significant (AUC=0.746 [95% CI=0.665–0.826],  $p < 0.001$ ), neutrophil's significant (AUC=0.771 [95% CI=0.691–0.851],  $p < 0.001$ ), NLR's significant (AUC=0.735 [95% CI=0.616–0.854],  $p < 0.001$ ), NPR's significant (AUC=0.789 [95% CI=0.703–0.874],  $p < 0.001$ ), and IGLR's significant (AUC=0.712 [95% CI=0.592–0.833],  $p < 0.001$ ) efficacies were observed (Table 3).

In differentiating between the UCAA and CAA patients, the following parameters were observed to have significant efficacy: IG (AUC=0.737 [95% CI=0.652–0.821]  $p < 0.001$ ), CRP (AUC=0.747 [95% CI=0.656–0.837]  $p < 0.001$ ), NLR (AUC=0.742 [95% CI=0.653–0.831]  $p < 0.001$ ), PLR (AUC=0.707 [95% CI=0.607–0.806]  $p < 0.001$ ), IGLR (AUC=0.782 [95% CI=0.698–0.865]  $p < 0.001$ ), PLR (AUC=0.731 [95% CI=0.646–0.816]  $p < 0.001$ ), MLR (AUC=0.720 [95% CI=0.631–0.808]  $p < 0.001$ ), and RDWLR (AUC=0.711 [95% CI=0.617–0.806]  $p < 0.001$ ) (Table 3).

## DISCUSSION

One of the most common causes of emergency surgery is AA. Today, the usability of non-operative treatment meth-

**Table 2.** Variables in the univariate and multivariate regression model distinguishing between negative appendectomy positive appendectomy and uncomplicated acute appendicitis complicated acute appendicitis groups

	Negative appendectomy/Positive appendectomy						Uncomplicated AA/Complicated AA					
	Univariate model			Multivariate model			Univariate model			Multivariate model		
	OR	95% CI	p	OR	95% CI	p	OR	95% CI	p	OR	95% CI	p
WBC	1.25	1.12–1.41	<0.001				1.14	1.05–1.24	0.001			
PLT	1.00	0.99–1.00	0.278				1.00	1.00–1.01	0.374			
Neutrophil	1.32	1.16–1.51	<0.001				1.18	1.09–1.29	<0.001			
Lymphocyte	0.83	0.66–1.04	0.103				0.44	0.27–0.71	<0.001			
Monocyte	4.59	1.36–15.55	0.014				1.62	0.73–3.59	0.239			
RDW-CV	1.28	0.85–1.92	0.231				1.13	0.93–1.38	0.208			
IG	>200	>200–>200	0.008				>200	>200–>200	<0.001			
CRP	1.05	0.95–1.16	0.331				1.18	1.11–1.25	<0.001	1.14	1.07–1.22	<0.001
T.BIL	2.84	0.87–9.20	0.083				1.42	0.91–2.24	0.127			
NLR	1.25	1.07–1.47	0.005				1.16	1.09–1.22	<0.001			
PLR	1.00	1.00–1.01	0.241				1.00	1.00–1.01	<0.001			
NPR	>200	>200–>200	<0.001	>200	>200–>200	<0.001	>200	>200–>200	0.002			
IGLR	>200	>200–>200	0.008				>200	>200–>200	<0.001	>200	>200–>200	<0.001
MLR	7.43	1.20–46.11	0.031				4.19	1.89–9.31	<0.001			
RDWLR	1.09	0.97–1.23	0.159				1.08	1.03–1.13	0.001			

Logistic Regression (Forward LR). WBC: White blood cells; PLT: Platelets; RDW-CV: Red blood cell distribution width; IG: Immature granulocyte; CRP: C-reactive protein; T.BIL: Total bilirubin; NLR: Neutrophil-to-lymphocyte ratio; PLR: Platelet-to-lymphocyte ratio; NPR: Neutrophil-to-platelet ratio; IGLR: IG-to-Lymphocyte ratio; MLR: Monocyte-to-Lymphocyte Ratio; RDWLR: red blood cell distribution width-to-lymphocyte ratio; OR: Odds ratio; CI: Confidence interval.

ods in uncomplicated appendicitis cases has been evaluated in randomized controlled studies and found to be a good option.<sup>[9]</sup> This has led to the necessity of differentiating between CAA and UCAA cases more precisely at diagnosis. The most accepted diagnostic strategy for the disease is still clinical evaluation and routine laboratory assessments. However, false positivity in diagnosis is higher than the desired level and it is insufficient to determine the severity of AA. The low sensitivity and specificity in differentiation cause prolonged treatment, increased treatment costs, unnecessary risks, and increased morbidity.<sup>[4]</sup>

Imaging methods combined with clinical evaluation and laboratory findings have provided a significant reduction in the negative appendectomy rate.<sup>[10]</sup> Although radiological assessment maintains its importance in the diagnosis of AA, studies have revealed that cases classified as UCAA are likely to actually have CAA.<sup>[2]</sup> There is also the fact that access to imaging methods is not equally easy throughout the world. For instance, computerized tomography is expensive and also associated with increased radiation exposure. Scoring systems like the Alvarado Score and Appendicitis Inflammatory Response (AIR), which were developed to diagnose AA, demonstrate 94–99% success in predicting the absence of appendicitis. However, it has been reported that the Alvarado score is ineffective in differentiating between CAA

and UCAA, and the AIR scoring system is effective in such differentiation.<sup>[11]</sup>

Several studies have been conducted to evaluate the efficacy of routine diagnostic laboratory tests in the differentiation between NA and PA and between CAA and UCAA. We found that WBC, which was measured as part of the CBC test that was performed in almost all of the patients presenting to the emergency department with abdominal pain, had a high value for discriminating between NA and PA (AUC: 0.746). The discriminative value of neutrophils was even higher (AUC: 0.771). However, it is reported that the increase in WBC and the increase in neutrophils do not display the discriminatory power of efficacy they have in the diagnosis of AA in the differentiation between CAA and UCAA.<sup>[12]</sup> We reached a similar result in our study. We found the WBC and neutrophil counts to be significantly higher in the CAA group than in the UCAA group. We established a significant discrimination between the groups but it was weaker than many other parameters (AUC: 0.658 and 0.682). We found that the CRP value was relatively effective in differentiating between CAA and UCAA (AUC: 0.747,  $p < 0.001$ ). We further found that it was particularly effective in excluding CAA at a cut-off point of CRP  $> 7.55$ , with a sensitivity of 56.4%, and a specificity of 85.6%. Despite publications reporting that CRP is insufficient for this differentiation,<sup>[13]</sup> Parekh et al.<sup>[5]</sup> demonstrated a correlation between

**Table 3.** Results of the receiver operating characteristic analysis and sensitivity, specificity

	Negative appendectomy / Positive appendicitis					Uncomplicated AA/ Complicated AA						
	AUC	95% CI	p	Cut off	Sensitivity	Specificity	AUC	95% CI	p	Cut off	Sensitivity	Specificity
WBC	0.746	0.665-0.826	<0.001	13.52	57.6%	84.0%	0.658	0.573-0.744	0.001	14.84	71.8%	58.1%
PLT	0.413	0.302-0.524	0.148	350.00	6.8%	100.0%	0.548	0.450-0.647	0.327	302.50	33.3%	82.4%
Neutrophil	0.771	0.691-0.851	<0.001	9.135	68.7%	80.0%	0.682	0.595-0.769	<0.001	12.945	56.4%	69.7%
Lymphocyte	0.359	0.238-0.480	0.019	0.735	95.4%	8.0%	0.289	0.196-0.381	<0.001	0.575	100.0%	2.1%
Monocyte	0.675	0.576-0.773	0.004	0.785	65.6%	72.0%	0.547	0.457-0.637	0.342	0.835	74.4%	40.5%
RDW-CV	0.561	0.455-0.667	0.309	13.05	29.7%	84.0%	0.561	0.467-0.656	0.215	12.85	46.2%	64.1%
IG	0.687	0.567-0.806	0.002	0.025	88.2%	40.0%	0.737	0.652-0.821	<0.001	0.055	74.4%	60.6%
CRP	0.582	0.462-0.702	0.172	0.75	60.4%	56.0%	0.747	0.656-0.837	<0.001	7.55	56.4%	85.6%
T.BIL	0.607	0.490-0.725	0.073	0.495	77.1%	44.0%	0.610	0.522-0.697	0.026	0.555	87.2%	34.5%
NLR	0.735	0.616-0.854	<0.001	3.686	76.2%	72.0%	0.742	0.653-0.831	<0.001	11.064	56.4%	88.0%
PLR	0.581	0.467-0.695	0.177	171.987	28.5%	88.0%	0.707	0.607-0.806	<0.001	177.651	64.1%	77.8%
NPR (1/10 <sup>3</sup> )	0.789	0.703-0.874	<0.001	46.429	48.9%	96.0%	0.662	0.576-0.749	0.001	47.432	71.8%	58.1%
IGLR (1/10 <sup>3</sup> )	0.712	0.592-0.833	<0.001	8.43	93.5%	48.0%	0.782	0.698-0.865	<0.001	37.038	71.8%	74.3%
MLR	0.700	0.581-0.819	<0.001	0.303	81.1%	56.0%	0.720	0.631-0.808	<0.001	0.738	59.0%	81.3%
RDWLR	0.647	0.523-0.771	0.014	5.207	72.8%	60.0%	0.711	0.617-0.806	<0.001	8.157	66.7%	71.8%

ROC Curve, WBC: White blood cells; PLT: Platelets; RDW-CV: Red blood cell distribution width; IG: Immature granulocyte; CRP: C-reactive protein; T.BIL: Total bilirubin; NLR: Neutrophil-to-lymphocyte ratio; PLR: Platelet-to-lymphocyte ratio; NPR: Neutrophil-to-platelet ratio; IGLR: IG-to-Lymphocyte ratio; MLR: Monocyte-to-Lymphocyte Ratio; RDWLR: red blood cell distribution width-to-lymphocyte ratio; AUC: Area under curve; CI: Confidence interval.

CAA and elevated CRP. Korkut et al.<sup>[14]</sup> obtained similar findings, showing that CRP was effective (p<0.001) in differentiating between CAA and UCAA. However, the power of CRP for discriminating between the NA and PA groups in our study remains lower than its power in distinguishing complicated cases. The literature reports that the T.BIL value is effective in the differentiation between NA and PA, especially in AA patients with a normal WBC count.<sup>[15]</sup> It has been reported that hyperbilirubinemia (>1 mg/dl) can be used with a sensitivity of 54.3% and a specificity of 87.1% in predicting perforated appendicitis cases.<sup>[16]</sup> On the other hand, there are publications indicating that the T.BIL level does not have any diagnostic value.<sup>[5]</sup> In our study, although the T.BIL value differed significantly between the CAA and UCAA groups (p=0.026), it was not found to have enough efficacy in this differentiation when evaluated by the ROC analysis. A study by Ünal demonstrated that the IG count was an important parameter in the diagnosis of AA, as well as in the differentiation of CAA at a cut-off point of >0.104 (10<sup>3</sup>/uL), with a sensitivity of 93%, and specificity of 93.8%.<sup>[17]</sup> In our study, sensitivity was 74.4%, and specificity was 60.6% at a cutoff point IG >0.055 (10<sup>3</sup>/uL). However, we established that IG was an effective parameter (AUC: 0.737, p<0.001) in differentiating between CAA and UCAA, and was the laboratory result with the second highest discriminative value after CRP. This result strengthens the thesis that we will attain a higher discrimination when IG is used in the new parameters obtained with the calculated ratios.

There are laboratory parameters that increase and decrease in response to inflammatory processes. Using this difference between parameters, various ratios have been introduced to evaluate inflammatory response and to improve prediction. The NLR is one of the most studied ratios in the differentiation between CAA and UCAA. A meta-analysis by Hajibandeh et al.<sup>[8]</sup> in 2019 reported that NLR predicted the severity of appendicitis at a cut-off value of 8.8, with a sensitivity of 76.92% and specificity of 100%. On the discovery of PLT' effects on inflammation in addition to their hemostatic functions, ratios in-

cluding platelets as a parameter have also been introduced. The PLR was reported to predict CAA cases with high sensitivity (74.4%) and specificity (73.5%) (cutoff value: 169.7).<sup>[18]</sup> In line with the literature, our study found NLR to be quite effective in differentiating between NA and PA and between CAA and UCAA (AUC: 0.735 and 0.742). We established that PLR was effective in differentiating between CAA and UCAA (AUC: 0.707; cutoff: 177.65, sensitivity: 64.1%, specificity: 77.8%) but it could not display this efficacy in differentiation between NA and PA (AUC: 0.541).

To the best of our knowledge, there is no study in the literature regarding the NPR in patient groups with AA. It was used in cardiology studies that demonstrated the relationship between a high NPR rate and increased mortality in patients with infective endocarditis<sup>[19]</sup> and that showed its relationship with short- and long-term mortality in patients with ST-elevation myocardial infarction.<sup>[20]</sup> In these studies, the values of neutrophil and platelet in inflammatory response were considered. As another study group in patients with ischemic stroke; NPR ratio was used by evaluating the inflammatory function of neutrophil and hemostatic function of platelet. It has been shown that the increase in NPR is associated with hemorrhagic transformation in patients with acute ischemic stroke and is effective in predicting the prognosis of acute ischemic stroke.<sup>[21,22]</sup> When we evaluated our study group, NPR had high specificity in the differentiation between PA and NA groups, and had high positive predictive value (PPV) (AUC: 0.789; cutoff: 0.0464, sensitivity: 48.9%, specificity: 96.0%, and PPV: 99.4%). However, it was not at the desired level in the differentiation of complicated cases.

IG is an inflammatory marker indicating bone marrow activity and severe infection, which is not sufficiently known by many clinicians.<sup>[23]</sup> Although the efficiency of IG count in the diagnosis of AA and the differentiation between UCAA and CAA has been shown in the literature,<sup>[17]</sup> there is a limited number of studies that use indirect results obtained by proportioning to other parameters to increase this efficacy. Among these, a study by Korkut et al.<sup>[14]</sup> established that the IG-to-neutrophil ratio was insufficient for the diagnosis of AA and complicated appendicitis. We believe that proportioning two parameters that are expected to elevate in the inflammation process is an erroneous approach and the most important reason for statistical insignificance. With this understanding, we preferred to evaluate the IGLR in our patient group. When we compared the NA and PA groups, the predictive values of IGLR ratio were sufficient (AUC: 0.712). However, the result is still behind the NPR and NLR ratios. Despite all these findings, we found that between CAA and UCAA groups, IGLR had higher selectivity and negative predictive value (NPV), than all other evaluated parameters (AUC: 0.782; cutoff:  $37.038 \cdot 10^{-3}$ , sensitivity: 71.8%, specificity: 74.3%, and NPV: 95%). In the light of the literature and our findings showing that IG was more effective in differentiating between CAA and UCAA, our results were not surprising. Considering that NPR is also less selective

than NLR, we conclude that the selectivity of the reduced lymphocyte count in complicated cases increases the prediction more. Another reason for this finding is that the platelet count did not differ between the NA, UCAA, and CAA groups.

Some other parameters obtained by CBC have lower clinical value in the diagnosis of AA or in the differentiation of CAA. In a study by Boshnak et al.,<sup>[24]</sup> the red cell distribution width (RDW) level was found to be significantly higher in complicated patients than in those with UCAA, but no significant difference was established between the AA and NA groups. Our study did not find any significant difference between the groups. In the literature, we have not come across any study using the RDWLR in patients with AA. A study on a group of patients with colorectal cancer (CRC) reported that the RDWLR ratio was higher in CRC patients than in the control group and was significantly higher in the presence of advanced stage and distant metastasis.<sup>[25]</sup> In our study, the ROC analysis revealed that the efficacy of RDWLR in the differentiation between CAA and UCAA was close to the levels of NLR and PLR (AUC: 0.711, cutoff: 8.157, sensitivity: 66.7%, and specificity: 71.8%). The cutoff value and specificity found in our study were similar to those reported by Huang et al.<sup>[25]</sup> in the differentiation of CRC patients, while our sensitivity result was better. However, the efficacy of RDWLR in differentiating between NA and PA remained low (AUC: 0.647).

It has been shown that NLR and MLR are highly correlated with each other, and high values of both NLR and MLR are associated with bacterial infections.<sup>[26]</sup> A study that used the lymphocyte-to-monocyte ratio instead of MLR found it to be significantly lower in the group of patients with AA than in the group with FMF.<sup>[27]</sup> In our study, MLR was effective in differentiating between NA and PA (AUC: 0.700) and between CAA and UCAA (AUC: 0.720). However, the AUC values were below the IGLR and NLR efficacies in both comparisons.

The most important limitation of our study is its retrospective design. Differences in the calibration values of laboratory devices are a limiting factor that should be considered, although similar results were obtained in different studies. Furthermore, the negative appendectomy and CAA groups were more limited in number. We will be following new prospective studies in larger cohorts.

## Conclusion

In our study, we evaluated the NPR, IGLR and RDWLR, which have not been previously evaluated in AA disease and in differentiation of CAA-UCAA, and we found that these parameters to be statistically significant in these differentiations. While the neutrophil count and the NLR and NPR values, obtained using the neutrophil count, showed a high level of prediction in the differentiation between NA and PA, the IG count and the IGLR value obtained using the IG count had a higher predictive value in differentiating between

UCAA and CAA. It was found that none of the laboratory parameters that could assist in the differentiation had sensitivity and specificity at the level of a gold standard. However, we recommend the use of NPR in the differentiation of the NA group in patients with a pre-diagnosis of AA due to its specificity of 96.0% and PPV of 99.4%, and the use of IGLR in the differentiation of the UCAA cases due to its sensitivity of 71.8%, specificity of 74.3%, and NPV of 95%. Despite their statistical significance, the clinical use of NPR and IGLR is limited. We hope that our study will guide other studies that will investigate the usability of these parameters.

**Ethics Committee Approval:** This study was approved by the Alanya Alaaddin Keykubat University Faculty of Medicine Clinical Research Ethics Committee (Date: 13.01.2021, Decision No: 01-15).

**Peer-review:** Internally peer-reviewed.

**Authorship Contributions:** Concept: M.K.; Design: M.K.; Supervision: S.Ş.; Resource: M.K., S.Ş.; Data: M.K., S.Ş.; Analysis: M.K., S.Ş.; Literature search: M.K., S.Ş.; Writing: M.K., S.Ş.; Critical revision: M.K., S.Ş.

**Conflict of Interest:** None declared.

**Financial Disclosure:** The authors declared that this study has received no financial support.

## REFERENCES

- Ruffolo C, Fiorot A, Pagura G, Antoniutti M, Massani M, Caratozzolo E, et al. Acute appendicitis: What is the gold standard of treatment? *World J Gastroenterol* 2013;19:8799–807. [CrossRef]
- Vons C, Barry C, Maitre S, Pautrat K, Leconte M, Costaglioli B, et al. Amoxicillin plus clavulanic acid versus appendicectomy for treatment of acute uncomplicated appendicitis: An open-label, non-inferiority, randomised controlled trial. *Lancet* 2011;377:1573–9. [CrossRef]
- Gorter RR, Eker HH, Gorter-Stam MA, Abis GS, Acharya A, Ankersmit M, et al. Diagnosis and management of acute appendicitis. EAES consensus development conference 2015. *Surg Endosc* 2016;30:4668–90. [CrossRef]
- Young KA, Neuhaus NM, Fluck M, Blansfield JA, Hunsinger MA, Shahbahang MM, et al. Outcomes of complicated appendicitis: Is conservative management as smooth as it seems? *Am J Surg* 2018;215:586–92.
- Parekh D, Jain D, Mohite S, Phalgune D. Comparison of outer diameter of appendix, C-reactive protein, and serum bilirubin levels in complicated versus uncomplicated appendicitis. *Indian J Surg* 2020;82:314–8. [CrossRef]
- Atema JJ, van Rossem CC, Leeuwenburgh MM, Stoker J, Boermeester MA. Scoring system to distinguish uncomplicated from complicated acute appendicitis. *Br J Surg* 2015;102:979–90. [CrossRef]
- Chambers A, Bismohun S, Davies H, White P, Patil A. Predictive value of abnormally raised serum bilirubin in acute appendicitis: A cohort study. *Int J Surg* 2015;13:207–10. [CrossRef]
- Hajibandeh S, Hajibandeh S, Hobbs N, Mansour M. Neutrophil-to-lymphocyte ratio predicts acute appendicitis and distinguishes between complicated and uncomplicated appendicitis: A systematic review and meta-analysis. *Am J Surg* 2020;219:154–63. [CrossRef]
- Salminen P, Tuominen R, Paajanen H, Rautio T, Nordström P, Aarnio M, et al. Five-year follow-up of antibiotic therapy for uncomplicated acute appendicitis in the APPAC randomized clinical trial. *JAMA* 2018;320:1259–65. [CrossRef]
- Raja AS, Wright C, Sodickson AD, Zane RD, Schiff GD, Hanson R, et al. Negative appendectomy rate in the era of CT: An 18-year perspective. *Radiology* 2010;256:460–5. [CrossRef]
- Yeşiltaş M, Karakaş DÖ, Gökçek B, Hor S, Eğin S. Can Alvarado and appendicitis inflammatory response scores evaluate the severity of acute appendicitis? *Ulus Travma Acil Cerrahi Derg* 2018;24:557–62. [CrossRef]
- Coleman C, Thompson JE Jr., Bennion RS, Schmit PJ. White blood cell count is a poor predictor of severity of disease in the diagnosis of appendicitis. *Am Surg* 1998;64:983–5.
- Biricik S, Narci H, Dündar GA, Ayrık C, Türkmenoğlu MÖ. Mean platelet volume and the ratio of mean platelet volume to platelet count in the diagnosis of acute appendicitis. *Am J Emerg Med* 2019;37:411–4.
- Korkut M, Bedel C, Selvi F. Are immature granulocytes and derivatives early predictors of acute appendicitis and acute complicated appendicitis in adults? *Formos J Surg* 2020;53:123. [CrossRef]
- Birben B, Akkurt G, Akin T, Surel AA, Tez M. Efficacy of bilirubin values in diagnosing acute appendicitis in patients with normal white blood cell count and predicting complicated appendicitis. *Ulus Travma Acil Cerrahi Derg* 2021;27:50–4. [CrossRef]
- Hussain MT, Syed S, Ijaz H, Ali A, Khan E, Khan K. Accuracy of hyperbilirubinemia and neutrophil lymphocyte ratio as independent predictors of perforation in acute appendicitis. *Rawal Med J* 2020;45:410–3.
- Ünal Y. A new and early marker in the diagnosis of acute complicated appendicitis: Immature granulocytes. *Ulus Travma Acil Cerrahi Derg* 2018;24:434–9. [CrossRef]
- Yıldırım AC, Anuk T, Günel E, İrem B, Gülkan S. Clinical value of the platelet-to-lymphocyte ratio for diagnosing complicated acute appendicitis. *Turk J Colorectal Dis* 2017;27:1–5. [CrossRef]
- Wei XB, Liu YH, He PC, Yu DQ, Tan N, Zhou YL, et al. The impact of admission neutrophil-to-platelet ratio on in-hospital and long-term mortality in patients with infective endocarditis. *Clin Chem Lab Med* 2017;55:899–906. [CrossRef]
- Somaschini A, Cornara S, Demarchi A, Mandurino-Mirizzi A, Fortuni F, Crimi G, et al. Neutrophil to platelet ratio: A novel prognostic biomarker in ST-elevation myocardial infarction patients undergoing primary percutaneous coronary intervention. *Eur J Prev Cardiol* 2020;27:2338–40.
- He W, Ruan Y, Yuan C, Cheng Q, Cheng H, Zeng Y, et al. High neutrophil-to-platelet ratio is associated with hemorrhagic transformation in patients with acute ischemic stroke. *Front Neurol* 2019;10:1310. [CrossRef]
- Jin P, Li X, Chen J, Zhang ZR, Hu WW, Chen LY, et al. Platelet-to-neutrophil ratio is a prognostic marker for 90-days outcome in acute ischemic stroke. *J Clin Neurosci* 2019;63:110–5. [CrossRef]
- Park JS, Kim JS, Kim YJ, Kim WY. Utility of the immature granulocyte percentage for diagnosing acute appendicitis among clinically suspected appendicitis in adult. *J Clin Lab Anal* 2018;32:e22458. [CrossRef]
- Boshnak N, Boshnaq M, Elgohary H. Evaluation of platelet indices and red cell distribution width as new biomarkers for the diagnosis of acute appendicitis. *J Invest Surg* 2018;31:121–9. [CrossRef]
- Huang J, Zhao Y, Liao L, Liu S, Lu S, Wu C, et al. Evaluation of red cell distribution width to lymphocyte ratio as potential biomarker for detection of colorectal cancer. *Biomed Res Int* 2019;2019:9852782. [CrossRef]
- Naess A, Nilssen SS, Mo R, Eide GE, Sjørnsen H. Role of neutrophil to lymphocyte and monocyte to lymphocyte ratios in the diagnosis of bacterial infection in patients with fever. *Infection* 2017;45:299–307. [CrossRef]
- Tuncer AA, Cavus S, Balcioglu A, Silay S, Demiralp I, Calkan E, et al. Can mean platelet volume, neutrophil-to-lymphocyte, lymphocyte-to-monocyte, platelet-to-lymphocyte ratios be favourable predictors for the differential diagnosis of appendicitis. *J Pak Med Assoc* 2019;69:647–53.

## ORIJİNAL ÇALIŞMA - ÖZ

**Komplike akut apandisit ayırt etmede nötrofil-trombosit oranının, immature granülosit-lenfosit oranının, eritrosit dağılımı genişliği-lenfosit oranının değeri****Dr. Mehmet Kubat,<sup>1</sup> Dr. Serkan Şengül<sup>2</sup>**<sup>1</sup>Alanya Eğitim ve Araştırma Hastanesi, Genel Cerrahi Kliniği, Antalya<sup>2</sup>Alanya Alaaddin Keykubat Üniversitesi Tıp Fakültesi, Genel Cerrahi Anabilim Dalı, Antalya

**AMAÇ:** Komplike olmayan akut apandisit olgularında tıbbi tedavi başarısının olabileceğinin anlaşılması üzerine, komplike akut apandisit olgularının başarılı bir şekilde ayırt edilmesi gerekliliği ortaya çıkmıştır. Çalışmamızda, nötrofil/trombosit oranı, immatür granülosit/lenfosit oranı, eritrosit dağılımı genişliği/lenfosit oranı parametrelerinin komplike-komplike olmayan akut apandisit olgularının ayırımıdaki kullanılabilirliği irdelemektedir.

**GEREÇ VE YÖNTEM:** Ocak 2019/Aralık 2020 tarihleri arasında apendektomi yapılan hastalar geriye dönük olarak değerlendirildi. Patolojik ve klinik bulgulara göre negatif apendektomi, komplike akut apandisit ve komplike olmayan akut apandisit gruplarına ayrıldı. Laboratuvar parametreleri ve bu parametrelerden elde edilen oranlar gruplar arasında değerlendirildi.

**BULGULAR:** Çalışmaya 348 hasta alındı. Hastaların %11.2'sinin komplike akut apandisit, %81.6'sının komplike olmayan akut apandisit ve %7.2'sinin negatif apendektomi olduğu görüldü. Komplike-komplike olmayan akut apandisit ayırımı; nötrofil/lenfosit oranı (AUC=0.742), trombosit/lenfosit oranı (AUC=0.707), immatür granülosit/lenfosit oranı (AUC=0.782), monosit/lenfosit oranı (AUC=0.720) ve eritrosit dağılımı genişliği/lenfosit oranı (AUC=0.711) anlamlı bulundu. Nötrofil/trombosit oranı (AUC=0.789) pozitif apendektomi-negatif apendektomi ayırımıda anlamlı bulundu.

**TARTIŞMA:** Daha önce akut apandisit tanılı olgularda çalışılmamış olan immatür granülosit/lenfosit oranı, nötrofil/trombosit oranı, monosit/lenfosit oranı, eritrosit dağılımı genişliği/lenfosit oranı parametreleri; komplike akut apandisit-komplike olmayan akut apandisit grupları ayırımıda kullanılabilir oldukları sonucuna varıldı.

**Anahtar sözcükler:** Akut apandisit; eritrosit dağılımı genişliği/lenfosit oranı; immatür granülosit/lenfosit oranı; komplike apandisit; monosit/lenfosit oranı; nötrofil/trombosit oranı.

Ulus Travma Acil Cerrahi Derg 2022;28(5):607-614 doi: 10.14744/tjes.2021.30434