

# Are the immature granulocyte count and percentage important in continue medical treatment in acute appendicitis? A prospective, randomized, and controlled study

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## ABSTRACT

**BACKGROUND:** Although appendectomy is still a curative therapy for acute appendicitis, medical treatment has come to the fore in uncomplicated cases. This study aimed to determine the importance of immature granulocyte (IG) count and percentage for the role of medical treatment success in uncomplicated acute appendicitis.

**METHODS:** Acute appendicitis cases were prospectively registered between July 2019 and April 2020. Using ball drawing, patients were divided into two groups as medical treatment (Group M) and undergo appendectomy (Group A). Group M was divided into two subgroups as those who responded to medical treatment medically responded (MR) and failed medical treatment (MF) within 24 h of follow-up. Changes in IG count and percentage, C-reactive protein levels, neutrophil-lymphocyte ratio, and white blood cell count between initial administration and 24<sup>th</sup> h of follow-up were examined.

**RESULTS:** Sixty-four patients who met the inclusion criteria were followed as 31 patients in Group A and 33 in Group M. At Subgroup MF 11 patients and Subgroup MR 22 patients were followed up. At the 24<sup>th</sup> h of the follow-up, the IG count and percentage were higher in the Group MF (for IG count: Between Group A and MF,  $p=0.002$ ; between Group A and Group MR,  $p=0.111$ ; and between Group MR and MF,  $p<0.001$ ) (for IG percentage: Between Group A and MF,  $p=0.001$ ; between Group A and MR,  $p=0.809$ ; and between Group MF and MR,  $p=0.001$ ). This decrease in the IG count and percentage suggests that the response to medical treatment was effective [for IG count:  $F(148.862) = 61$ ,  $p\leq 0.001$ ,  $\eta^2=0.707$ ] [for IG percentage:  $F(10.157) = 0.252$ ,  $p\leq 0.001$ ,  $\eta^2=0.504$ ].

**CONCLUSION:** IG count and percentage are effective for evaluating the success of medical treatment of uncomplicated acute appendicitis and they guide in the decision to continue medical treatment of uncomplicated acute appendicitis.

**Keywords:** Delta neutrophile index; immature granulocyte count; immature granulocyte percentage; neutrophile lymphocyte ratio; non-operative management of uncomplicated acute appendicitis; uncomplicated acute appendicitis.

## INTRODUCTION

After appendectomy was first described by Mcburney in 1889, it has been one of the most practiced emergency sur-

gery in the world with the lifetime incidence of acute appendicitis being 5–25%.<sup>[1,2]</sup> Most cases are simple cases without any complications and perforation rates are between 20% and 30%.<sup>[3,4]</sup> Although appendectomy is still a curative thera-

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py, medical treatment has come to the fore in uncomplicated cases after improvements in imaging methods for diagnosing acute appendicitis and especially the developments in antibiotherapy.<sup>[1,2,5]</sup>

Medical treatment for acute appendicitis is, in fact, not a new condition. Practicing the option of elective surgery following intravenous antibiotherapy for plastron appendicitis that is among the complicated acute appendicitis has led to further consideration of medical treatment.<sup>[6,7]</sup> Medical treatment of diverticulitis, which is an inflammatory condition other than acute appendicitis, suggests that the medical treatment option may be preferred for uncomplicated acute appendicitis.<sup>[1,2,6]</sup> A number of studies conducted for this purpose suggest that conservative treatment in uncomplicated acute appendicitis may be a first-line treatment.<sup>[1,2,8,9]</sup> Indeed, there are a certain difficulties at this point; the most important of these is the complication of the cases of uncomplicated acute appendicitis because of prolonged conservative treatment, and consequently the increased risk of infectious complications (such as wound site infections and wound degradation).<sup>[1]</sup> Despite these potentially negative consequences, medical treatment of the cases of uncomplicated acute appendicitis prevents negative appendectomies, which indicates that surgical removal of non-inflamed appendix ranging from 6% to 20%. In addition to preventing unnecessary organ loss, it ensures eliminating post-operative complications such as intestinal obstruction (IO) and wound site complications because of surgery.<sup>[1,6,8,9]</sup>

Immature granulocytes (IG) are monitored in peripheral blood as immature polymorphonuclear cells because of the activation of bone marrow.<sup>[3]</sup> Although their counts can be determined through direct inspection, they can be provided with automated systems within complete blood count parameters as well as technological developments.<sup>[3,10]</sup> The increase in their number specifically suggests the activation of the bone marrow and can provide information about the infectious process before leukocytosis is observed.<sup>[11]</sup> For this purpose, in the separation of complicated and uncomplicated acute appendicitis, inflammatory events such as sepsis and acute pancreatitis have been studied before.<sup>[3,10-13]</sup>

In this context, questions such as how long medical treatment will be applied and when to decide on the surgery are an important problem. To evaluate the success of medical treatment, the change in white blood cell (WBC) levels and C-reactive protein (CRP) levels has been demonstrated to be significant.<sup>[2]</sup> However, it is an additional cost to study CRP as a separate parameter from the complete blood count.

This study aimed to determine the importance of IG count and percentage to evaluate the role of medical treatment and control its success in cases of uncomplicated acute appendicitis.

## MATERIALS AND METHODS

After approval of Local Ethics Committee (Kahramanmaraş Sütçü İmam University Bioethics Committee, for the study with protocol number 179; dated June 19, 2019; session no. 2019/11; and decision no.: 4), our study was organized as a 1-year prospective and randomized study. As a criterion for terminating the study, reaching the total number of patients obtained through power analysis. In the primary study endpoint, to detect a 20% difference with  $\alpha=5\%$  and  $\beta=20\%$ , a total sample size of 64 patients was reported to be necessary for achieving statistical significance. All procedures performed in studies involving human participants were in accordance with the ethical standards of the Institutional and/or National Research Committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Patients with the diagnosis of acute appendicitis over the age of 18 and treated by the same surgical team were prospectively registered to Kahramanmaraş Sütçü İmam University General Surgery Clinic between July 2019 and April 2020. Acute appendicitis was diagnosed with history, physical examination results, laboratory results, and imaging methods (Ultrasonography or Computed Tomography). As per these results, patients with Alvarado Score 7 and above were diagnosed with acute appendicitis.<sup>[6,8,14,15]</sup> Patients diagnosed with complicated acute appendicitis based on imaging methods (such as perforation, periappendicular abscess formation, and plastron formation), patients who are pregnant, and patients who did not want to be included were excluded from the study. Patients were informed that there were medical treatment and surgical treatment options in uncomplicated acute appendicitis and written consent was obtained from patients. For randomization purposes, patients were given balls to draw. Using this ball drawing, patients were divided into two groups as those that would receive random medical treatment (Group M) and those that would undergo direct appendectomy (Group A) (Open appendectomy or laparoscopic appendectomy). Group M was divided into two subgroups as those who responded to medical treatment within 24 h of follow-up and those who failed medical treatment. The study was terminated as the total number of 64 patients was reached because of power analysis.

In Group A, after examining the patient in the emergency, the patient was urgently taken to operation to perform appendectomy (open or laparoscopic). A complete blood count and CRP were studied on patients within the first 24 h of the post-operative course. In Group M, oral intake was discontinued on admission of patients to the clinic and intravenous ciprofloxacin (200 mg; twice a day) and metronidazole (500 mg; 3 times a day), which were effective for both Gram-positive and Gram-negative bacteria and anaerobes, were started with fluid replacement.<sup>[7]</sup> When the duration of non-surgical follow-up is between 12 and 24 h, there is no increase in the perforation risk. Considerable complications can be

encountered after 48 h (wound site infections, wound decomposition, and other complications).<sup>[6]</sup> Therefore, because of increased risk of perforation and the likelihood of complications as a result, the response protocol for medical treatment was restricted to 24 h. During follow-up, vital signs of patients were verified every 6 h. At the 24<sup>th</sup> h of follow-up, the patients were asked for their complaints and physical examinations were performed. Control of complete blood count, CRP, and abdominal US were performed. At the 24<sup>th</sup> h of the follow-up, Alvarado score was repeated to patients. Patients who had no regression in the clinic and laboratory results (with an Alvarado score  $\geq 7$  and who had an appendix unresponsive to medical treatment) according to the imaging methods (with no change in diameter or increased or developed complications) were considered to be unresponsive to medical treatment and rescue appendectomy was performed. These patients were divided into subgroup failed medical treatment (Group MF). Patients with a regression in physical examination and laboratory results (with calculating Alvarado score  $< 7$ ) and those with an appendix that responded to medical treatment as per imaging methods (with reduced diameter or not monitored with US) were considered to have responded to medical treatment; and oral intake was initiated without surgery. These patients were divided into subgroup responded to medical treatment (Group MR). They were discharged from the hospital with a prescription of 1-week oral antibiotic regimen (a combination of oral ciprofloxacin 500 mg and oral metronidazole 500 mg 2 times daily (morning and evening). At the end of antibiotic therapy, patients were called for control.

WBC count, neutrophil count, lymphocyte count, IG count, and IG% were measured using an automated hematological analyzer (XN 3000; Sysmex Corp., Kobe, Japan) and CRP levels were measured using an automated biochemical analyzer (Cobas C-702 module, Roche Diagnostics, Basel, Sweden) from blood samples obtained at the initial admission to the emergency department and the 24<sup>th</sup> h of the follow-up. Neutrophil-lymphocyte ratio (NLR) levels were manually calculated. The IG fraction includes promyelocytes, myelocytes, and metamyelocytes but not band neutrophils or myeloblasts.<sup>[16,17]</sup> Moreover, delta neutrophil index (DNI) (IG percentage-%) is the IG count to WBC ratio.

### Statistical Evaluation

IBM Statistical Package for the Social Sciences for windows, Version 20.0 software package (IBM Corp., Armonk, NY, USA) was used to evaluate statistical data.

Kolmogorov–Smirnov test was performed for the suitability of patients for normal distribution. Based on their suitability for normal distribution, paired sample t-test was used to evaluate intragroup measurements in numerical data, while Student t-test and Mann–Whitney U test were used in intergroup evaluation. Comparing subgroup analysis was done

with analysis of variance (ANOVA) for numerical data. Repeated measurement ANOVA and Scheffe's post hoc test were used to evaluate the relationship between subgroups and appendectomy group. Note that Chi-square test and Fischer's exact test were used to evaluate the categorical data. Numerical data were given as median $\pm$ standard deviation (SD) (minimum-maximum) and categorical data were indicated in count (n) and percentages (%). Statistically,  $p < 0.05$  values were considered to be significant.

## RESULTS

During this study, among 151 patients who were admitted to our clinic with a diagnosis of acute appendicitis and were followed-up and treated, 64 of them who complied with study criteria and given consent to be admitted to the study were prospectively monitored. When patients were divided into random groups, 31 patients were followed in Group A and 33 in Group M. At Group M, medical treatment of 11 patients (17.2%) failed, while 22 patients (34.4%) were successful at the end of 24-h follow-up. The success rate of medical treatment was 66.6% (22/33). Moreover, rescue appendectomy was performed on 11 patients in the group with failed medical treatment. In one of these patients, perforation was observed on exploration. Based on pathological results, two of the remaining 10 patients had flagmenous appendicitis and seven had acute appendicitis. Moreover, pathology was not compatible with acute appendicitis in one patient (negative appendectomy ratio = 1/11) (Fig. 1). Furthermore, none of the 22 patients in the successful medical group who came for control on the 7th day had no recurrence in the clinic.

Note that 28 of the patients involved in the study (43.8%) were male and 36 (56.3%) were female. There was no statistically significant difference between groups in terms of gender ( $p = 0.512$ ). The mean age of the patients was  $35.36 \pm 14.11$  (18–87) years. There was no statistically significant difference between the ages of Group A and Group M ( $p = 0.4$ ) (Table I). Table I shows the demographic data and follow-up results of patients according to the groups.

During hospitalization, there was no statistically significant difference between Group A and Group M in terms of CRP levels ( $p = 0.08$ ). In addition, there was no statistically significant difference seen between subgroups analysis at first admission (between Group A and MF,  $p = 0.053$ ; between Group MR and Group A,  $p = 0.254$ ; and between Group MR and MF,  $p = 0.553$ ). At the 24<sup>th</sup> h of follow-up, CRP levels were significantly higher in the Group MF than Group MR but there were no significant difference seen between Group A with Group MF and Group MR (between Group A and MF,  $p = 0.362$ ; between Group A and MR,  $p = 0.428$ ; and between MF and MR  $p = 0.03$ ).

Furthermore, there was a no statistically significant difference seen between Group A and Group M in terms of NLR during hospitalization ( $p = 0.336$ ). While there was no signif-

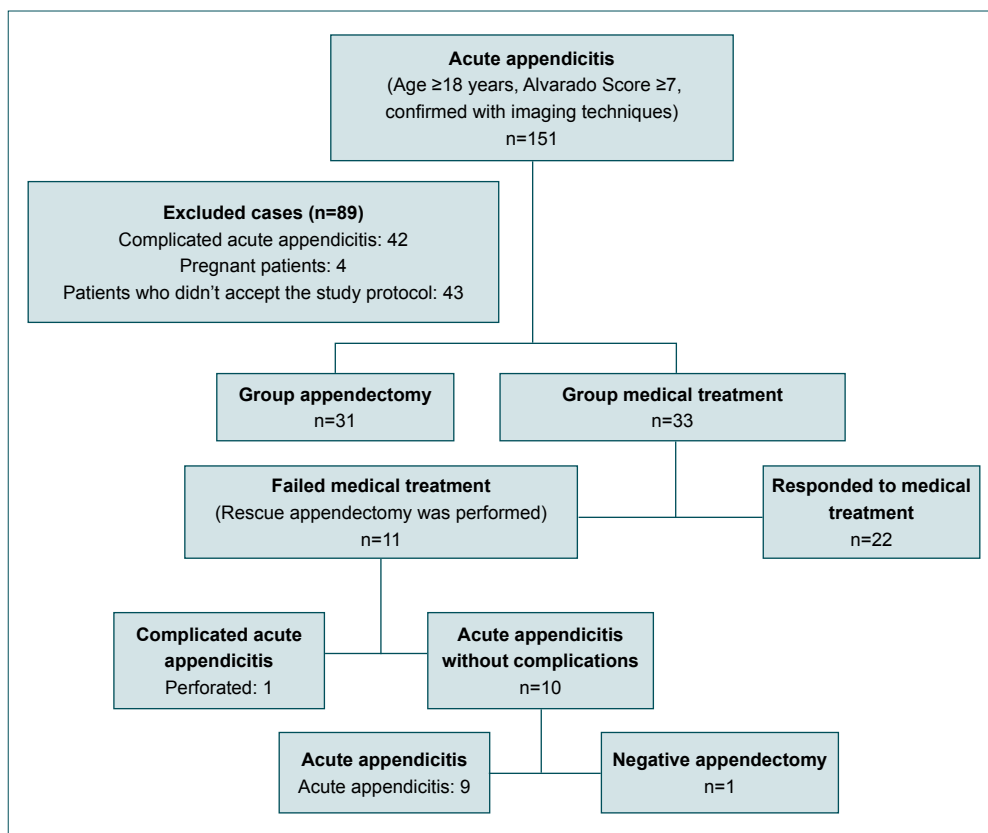


Figure 1. Flow chart of the results of the study.

icant difference between Group A and Group MF, Group MF and Group MR in terms of NLR at first admission, there was a statistically significant difference between Group A and Group MR at first admission (between Group A and MF,  $p=0.364$ ; between Group A and MR,  $p=0.007$ ; and between Group MF and MR,  $p=0.399$ ). At the 24<sup>th</sup> h of follow-up, in terms of NLR, in Group MR for NLR was significantly lower than both the group that Group A and Group MF (between Group A and Group MF,  $p=0.73$ ; among Group A and Group MR,  $p=0.002$ ; and between Group MF and MR,  $p=0.008$ ).

There was no a statistically significant difference between Group A and Group M seen in terms of the IG count during hospitalization ( $p=0.197$ ). However, there was not any statistical difference seen between Group A and Group MF, Group MR during the first admission period (between Group A and Group MF  $p=0.051$ ; between Group A and Group MR  $p=0.549$ ; and between Group MF and MR  $p=0.598$ ). At the 24<sup>th</sup> h of the follow-up, the IG count was significantly higher in Group MF (between Group A and MF,  $p=0.002$ ; between Group A and MR,  $p=0.111$ ; and between MF and MR,  $p<0.001$ ). This decrease in the IG count suggests that the response to medical treatment was effective [ $F(148.862) = 61, p<0.001, \eta^2=0.707$ ] (Table 2 and Fig. 2).

There was no statistically significant difference between Groups A and M in terms of IG% during hospitalization ( $p=0.246$ ). There was no significant difference between pa-

tients Group MF and MR and Group A in terms of the IG percentage in the pre-operative period (between Group A and MF,  $p=0.405$ ; between group A and MR,  $p=0.888$ ; and between Group MF and MR,  $p=0.262$ ). At the 24<sup>th</sup> h of follow-up, the IG percentage was significantly higher in the group with failed medical treatment (between Group A and MF,  $p=0.001$ ; between Group A and MR,  $p=0.809$ ; and between Group MF and MR,  $p=0.001$ ). This decrease in IG count showed response to medical treatment [ $F(10.157) = 0.252, p<0.001, \eta^2=0.504$ ] (Table 2 and Fig. 3).

### ROC Curve Analysis of IG Percentage (DNI), IG Count, NLR, and CRP Levels in Terms of Success in Medical Treatment in Acute Appendicitis at the 24<sup>th</sup> h of Follow-up

For diagnosing failed medical treatment, the cutoff value of IG percentage was  $\geq 0.35$  and its sensitivity and specificity were 75% and 75%, respectively (area under the curve [ARUC]: 0.828; confidence interval: 0.578–0.938; Positive Predictive Value (PPV): 72.7%; Negative Predictive Value (NPV): 77.3%) and the cutoff value of IG count was  $\geq 45$  and its sensitivity, specificity, PPV, and NPV were 75%, 87.5%, 75%, and 95.5%, respectively (ARUC: 0.858; TH: 0.578–0.938). ROC analyses of the parameters are shown in Table 2 and Figure 2.

In the follow-up period, a statistically significant difference was observed in the fever values of patients with Group

**Table 1.** Demographic data and follow-up results of patients

	Group A	Group M		p value
		Group MF	Group MR	
Total number of patients, n (%)	31 (48.4)	11 (17.2)	25 (34.4)	0.4
Male	14 (21.9)	7 (10.9)	10 (10.9)	
Female	11 (26.6)	4 (6.3)	15 (23.4)	
Age (years) [median±SD (min-max)]	34±14.13 (19–87)	33±12.62 (19–59)	30±15.21 (18–74)	0.634
Fever (°C) [median±SD (min-max)]				
0 h		36.7±0.09 (36.5–36.8)	36.65±0.19 (36–36.9)	0.56
6 h		36.7±0.2 (36.2–36.9)	36.8±0.18 (36.5–37.2)	0.012 <sup>c</sup>
12 h		36.8±0.17 (36.8–37.2)	36.8±0.34 (36.4–38.1)	0.188
18 h		37±0.25 (36.6–37.4)	36.7±0.37 (36–37.8)	0.007 <sup>c</sup>
24 h		37.2±0.36 (36.8–38)	36.6±0.17 (36.4–36.8)	<0.001 <sup>c</sup>
Alvarado Score [median±SD (min-max)]				
0 h	9±0.77 (7–9)	9±0.60 (7–9)	9±0.69 (7–9)	0.821
24 h		9±0.48 (8–9)	2±1.47 (1–6)	<0.001 <sup>c</sup>
WBC (10 <sup>3</sup> /mm <sup>3</sup> ) [median±SD (min-max)]				
0 h	13.94±4.38 (8.13–25.78)	10.81±2.32 (8.89–15.77)	12.30±3.88 (8.96–22.42)	0.171
24 h	9.5±2.96 (5.63–17.59)	13.83±3.69 (9.24–21.76)	8.32±2.05 (3.28–10.68)	0.424 <sup>b,c</sup>
CRP (mg/L) [median±SD (min-max)]				
0 h	36.4±89.79 (3–358)	4.5±15.66 (3–48.4)	20.6±73.88 (3.2–287)	0.08
24 h	18.9±54.21 (3–200)	48±99.60 (3.11–358)	9.30±46.66 (3.02–171)	0.217 <sup>c</sup>
IG count (/mm <sup>3</sup> ) [median±SD (min-max)]				
0 h	60±36.86 (20–180)	30±26.01 (10–100)	40±50.94 (10–210)	0.817
24 h	30±20.28 (10–90)	60±43.92 (30–180)	20±13.93 (10–60)	0.034 <sup>b,c</sup>
IG percentage (%) [median±SD (min-max)]				
0 h	0.4±0.22 (0.2–1.3)	0.3±0.19 (0.1–1.0)	0.4±0.33 (0.1–1.5)	0.143
24 h	0.3±0.13 (0.1–2.3)	0.5±0.16 (0.2–0.8)	0.3±0.12 (0.1–0.9)	0.001 <sup>b,c</sup>
NLR [median±SD (min-max)]				
0 h	6.09±4.44 (1.5–17.73)	4.34±3.86 (1.47–15.54)	3.35±3.32 (1.26–15.36)	0.336
24 h	4.47±5.45 (0.92–22.02)	5.21±4.73 (1.01–16.83)	2.36±1.44 (0.59–6.53)	0.005 <sup>b,c</sup>

<sup>a</sup>P<0.05; statistically significant difference observed between Group A and Group M according to the Mann–Whitney U test.

<sup>b</sup>P<0.05; statistically significant was observed between Group A and MR according to the Kruskal–Wallis Test.

<sup>c</sup>P<0.05; statistically significant was observed between Group A and MF group according to the Kruskal–Wallis Test.

<sup>d</sup>P<0.05; statistically significant was observed between Group MF and MR according to the Kruskal–Wallis Test.

Group A: Group appendectomy; Group M: Group medical treatment; Group MF: Failed Medical Treatment Group; Group MR: Responded to Medical Treatment Group; SD: Standard deviation; Min: Minimum value; Max: Maximum value; WBC: White blood cell count; CRP: C-reactive protein; IG: Immature granulocyte; NLR: Neutrophil to lymphocyte ratio.

MF and Group MR at the 6<sup>th</sup>, 18<sup>th</sup>, and 24<sup>th</sup> h of follow-up (Table 1).

According to the surgical exploration findings of Group MF, one patient developed complications (perforation). According to the pathological examination results of patients without complications, acute appendicitis in nine patients, and acute appendicitis was not observed in one patient (negative appendectomy: 1/11) (Table 3). When the pathological outcomes of Group A were examined, 25 patients were acute

appendicitis and 6 patients had no pathological findings compatible with acute appendicitis (negative appendectomy: 6/25) (Table 3). In the Group with MF, the negative appendectomy rate was significantly lower than Group A (p<0.001).

## DISCUSSION

Although medical treatment of acute appendicitis or, in other words, non-operative treatment of acute appendicitis is not a new subject, it still requires to be studied. In the second

**Table 2.** ROC analysis of failed medical treatment group at the 24<sup>th</sup> hour of the follow-up

Parameters	ARUC	Asymptotic 95% Confidence Interval		p-value	Sensitivity (%)	Spesivity (%)	Cut-off Value	PPV (%)	NPV (%)
		Lower bound	Upper bound						
IG Count (/mm <sup>3</sup> )	0.858	0.578	0.938	<0.001*	75	87.5	≥45	72.7	95.5
IG percentage (%)	0.828	0.571	0.925	0.001*	75	75	≥0.35	72.7	77.3
CRP (mg/L)	0.708	0.555	0.860	0.031*	72.7	67.9	≥25	72.7	81.8
NLR	0.638	0.46	0.817	0.277	63.6	60.4	≥3.69	63.6	81.8

\*P<0.05. ARUC: Area under curve; IG: Immature Granulocyte; CRP: C-reactive protein; NLR: Neutrophyl to lymphocyte ratio; PPV: Positive Predictive Value; NPV: Negative Predictive Value; ROC: Receiver Operating Characteristic.

**Table 3.** Pathological results of Group A and Group MF

	Group MF	Group A	Total
	n (%)	n (%)	n (%)
Acute appendicitis	9 (21.43)	25 (59.52)	34 (80.95)
Perforated acute appendicitis	1 (2.38)	0 (0)	1 (2.38)
Negative appendectomy	1 (2.38)	6 (14.29)	7 (16.67)
Total	11 (26.19)	31 (73.81)	42 (100)

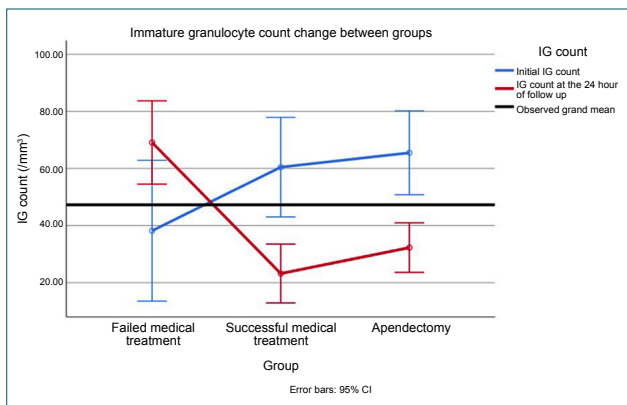
Group A: Appendectomy group; Group MF: Failed Medical Treatment Group.

quarter of 1900s, Bailey noted the algorithm of non-operative treatment of acute appendicitis.<sup>[18]</sup> Later on, Coldrey noted that medical treatment could be successful in patients with appendicular abscess and that antibiotherapy can be applied for other acute appendicitis<sup>[19]</sup>

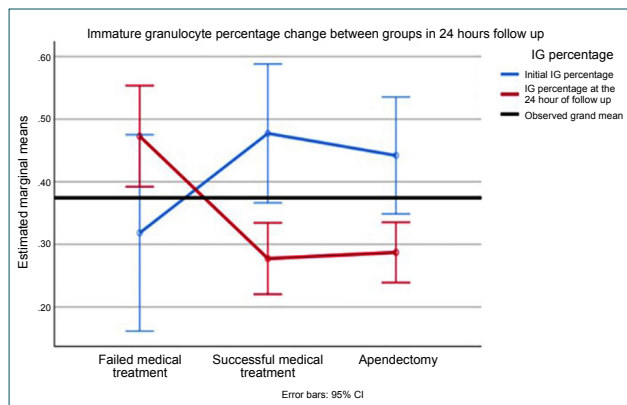
Appendectomy is currently the most effective treatment of acute appendicitis.<sup>[20]</sup> In the meta-analysis performed by Yang et al.,<sup>[9]</sup> they stated that although the conservative treatment of acute appendicitis is beneficial in adult patients and its complications are insignificantly lower than that of appen-

dectomy, the complication incidence is significantly lower than that of appendectomy. Tingstedt et al.<sup>[21]</sup> stated that the readmissions to the hospital increased after appendectomy; therefore, unnecessary appendectomies should be avoided to prevent this condition that occurs because of negative appendectomy. In their cohort study, Blomqvist et al.<sup>[22]</sup> stated that the mortality risk in non-perforated patients in the first 30-day post-operative period mortality increased 3.5-fold and in complicated cases, it increased 6.5-fold. However, they noted that, after negative appendectomy, these mortality rates increased 9.1-fold. Duron et al.<sup>[23]</sup> identified the prevalence of IO after open appendectomy as 0.35% in their studies that examined IO that occurred after laparoscopic surgery and open surgery. However, Zbar et al.<sup>[24]</sup> identified IO incidence as 10.7%. Because of surgical complications and increased mortality risk, the medical treatment in uncomplicated acute appendicitis has become a first-line treatment.

Although medical treatment has become more prominent in the treatment of uncomplicated acute appendicitis, its success should be evaluated. So what should we compare with? This is comparable to the pre-operative and post-operative outcomes of patients with appendectomy. Especially, in uncomplicated acute appendicitis cases, it is seen that the WBC, neutrophil count and CRP levels decrease in the labo-



**Figure 2.** Immature granulocyte count change among groups in the follow-up period.



**Figure 3.** Immature granulocyte percentage delta neutrophil index change among groups in the follow-up period.

ratory results that occur without complications after surgery.<sup>[25]</sup> Although studies evaluating the inflammatory response are mostly based on comparing open surgery with laparoscopic surgery, the decreases in these responses reflect appendectomies performed without complications. This led us to the idea that the success of patients with appendectomy and those with medical treatment can be compared in cases of uncomplicated acute appendicitis. In our study, it was observed that there was no difference in inflammatory response (WBC, NLR, CRP, DNI, and IG count) between the group in which successful medical treatment and the appendectomy group in the post-operative period, while a significant increase was observed in the group failed medical treatment. This situation showed us that the successful medical treatment can be evaluated as appendectomy and the inflammatory response was exacerbated in failed medical treatment.

When the medical treatment fails, the risk of developing complicated acute appendicitis increases. Moreover, because the tissue of the appendix is not removed, recurrence can be monitored.<sup>[1]</sup> In the study of 193 medical treatments conducted by the Okuş et al.,<sup>[2]</sup> they reported the failure rates as 13.51% (25/185) during 48–72 h of follow-up and stated that they did not encounter any complicated acute appendicitis in any patient undergoing rescue appendectomy. In a randomized controlled study on 45 diseases conducted by Ceresoli et al.,<sup>[26]</sup> they randomly directed patients to medical treatment or surgery and identified the failure rates in medical treatment as 15.8%, and stated that the negative appendectomy rates were 9.1% in patients undergoing direct appendectomy. In another study by Allievi et al.,<sup>[25]</sup> they indicated the failure rate of medical treatment as 1.8% during first admission to the hospital. Moreover, in a randomized and prospective study conducted by Svensson et al.,<sup>[27]</sup> the failure rate of medical treatment was 8%. Rescue appendectomy was performed on the patients who were included into the group with failed medical treatment on the 2<sup>nd</sup> day and 9<sup>th</sup> day of the follow-up. The pathology result of the patient who underwent appendectomy on day 2 was reported as lymphoid hyperplasia. Liu and Fogg stated that the failure rate ranged from 0% to 11.8% during 12–36 h of antibiotherapy administration.<sup>[28]</sup> In our study, the failure rate in medical treatment was 33% after 24-h follow-up, while the complicated acute appendicitis rate was 9.09% in patients who underwent rescue appendectomy. Our negative appendectomy rate was 14.29% in patients who underwent direct appendectomy and 9.09% in patients who underwent rescue appendectomy. We linked the fact that we had higher results than other studies in terms of failure in medical treatment to limiting our follow-up to 24 h.

There are multiple factors on which the failure of medical treatment depends. The high levels of CRP in the first administration, changes in CRP levels, the presence of intraluminal fecalith, age, changes in Alvarado score, and appendix diameter can be effective in this case.<sup>[2,6]</sup> In our study, higher IG count and DNI levels were observed for the failed medical

treatment at 24<sup>th</sup> h of the follow-up period. As higher levels of CRP, DNI and IG count can be predictive factor for fail of NOM of uncomplicated acute appendicitis cases in the follow-up period.

The evaluation of the success of medical treatment as per clinical evaluations, laboratory examinations, and results of imaging methods causes an increase in the requirement for examination.<sup>[29,30]</sup> With this increase, a requirement arises to evaluate success with a single parameter in follow-up. Okuş et al.<sup>[2]</sup> noted that CRP levels are an effective examination in tracking the success of medical treatment. However, performing this test requires additional costs. Measurement of IGs, which are leukocyte precursor cells resulting from activation of bone marrow, and DNI (IG%), which is the ratio of IG count to WBC count, is a useful marker of inflammation that enters routine complete blood count measurements.<sup>[15,16]</sup> The increased IG count and DNI are monitored in peripheral blood before the appearance of leukocytes for infection.<sup>[11]</sup> As is in Okuş et al., our study has demonstrated that changes in CRP levels are beneficial for monitoring the success of medical treatment. Furthermore, our study reported that the change in IG count and IG% was beneficial in assessing the success of the medical treatment for uncomplicated acute appendicitis cases. The decrease in IG count and IG% was a significant guide in continuing treatment.

### Limitations

The major limitation of our study is considered to ensure lower follow-up time. Although it is noted that the probability of developing complications is increasing after the first 24 h, the number of complicated cases in our study was not high. This was consistent with the study of Kirkil et al.,<sup>[12]</sup> which indicated that the probability of developing complications did not increase when the follow-up period was extended to 48–72 h. Moreover, because of our reduced follow-up period, the failure rates of medical treatment were seemed to be higher. This preliminary study can be supported with additional prospective and multicenter studies including greater number of patients and automatically calculated IG count and percentage can be more predictive for following the success of medical treatment.

### Conclusion

IG count and IG% are effective for evaluating the success of medical treatment of uncomplicated acute appendicitis and they are easily accessible blood parameters that do not incur additional costs because they are studied with automated systems within the complete blood count parameters. In addition, the IG count and IG% are an important guide in the decision to continue medical treatment of uncomplicated acute appendicitis.

**Ethics Committee Approval:** This study was approved by the Kahramanmaraş Sütçü İmam University Faculty

of Medicine Clinical Research Ethics Committee (Date: 19.06.2019, Decision No: 179/4).

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ORJİNAL ÇALIŞMA - ÖZ

## Akut apandisitinin tıbbi tedavisinin devam edilmesinde immatür granülosit sayısı ve yüzdesi önemli mi? İleriye yönelik randomize kontrollü çalışma

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**AMAÇ:** Her ne kadar apendektomi akut apandisitte halen küratif tedavi olsa da, komplike olmamış olgularda tıbbi tedavi ön plana çıkmaktadır. Bu çalışmada immatür granülosit (IG) sayısı ve yüzdesinin komplike olmamış akut apandisitinin tıbbi tedavisinin başarısındaki rolünün değerlendirilmesi amaçlandı.

**GEREÇ VE YÖNTEM:** Temmuz 2019 ile Nisan 2020 tarihleri arasında akut apandisit olguları ileriye yönelik olarak kayıt edildi. Hasta seçiminde top çekme kullanılarak hastalar tıbbi tedavi grubu (Grup M) ve apendektomi grubu (Grup A) olarak ikiye ayrıldı. Grup M, takibin 24. saatinde tıbbi tedavinin başarılı olduğu (Grup MR) ve olmadığı (Grup MF) olmak üzere iki alt gruba ayrıldı. Başvuru anındaki ve takibin 24. saatindeki IG sayısı ve yüzdesi, C-reaktif protein (CRP) düzeyleri, nötrofil lenfosit oranları ve beyaz küre değerlerindeki değişimler incelendi.

**BULGULAR:** Çalışmaya dahil olma kriterlerini karşılayan 64 hasta çalışmaya alınarak 31 hasta Grup A'da ve 33 hasta Grup M'de takip edildi. Alt grup incelemesinde Grup MF'de 11 hasta yer alırken Grup MR'de 22 hasta izlendi. Takibin 24. saatinde IG sayısı ve yüzdesi Grup MF'de diğer gruplara oranla yüksek izlendi (IG sayısı için: Grup A ile Grup MF,  $p=0.002$ ; Grup A ile Grup MR,  $p=0.111$ ; Grup MR ile Grup MF,  $p<0.001$ ) (IG yüzdesi için: Grup A ile Grup MF,  $p=0.001$ ; Grup A ile Grup MR,  $p=0.809$ ; Grup MF ile Grup MR,  $p=0.001$ ). Grup MR'de izlenen IG sayısı ve yüzdesindeki azalma IG sayısı ve yüzdesinin etkili olduğunu gösterdi [IG sayısı için:  $F(148.862)=61$ ,  $p<0.001$ ,  $\eta^2=0.707$ ] [IG yüzdesi için:  $F(10.157)=0.252$ ,  $p<0.001$ ,  $\eta^2=0.504$ ].

**TARTIŞMA:** IG sayısı ve yüzdesi komplike olmamış akut apandisit olgularında tıbbi tedavinin başarısını değerlendirmede etkilidir ve komplike olmamış akut apandisit olgularında tıbbi tedavinin devam edilmesine yol göstermektedir.

**Anahtar sözcükler:** Delta nötrofil indeksi; immatür granülosit sayısı; immatür granülosit yüzdesi; komplike olmamış akut apandisit; komplike olmamış akut apandisitinin nonoperatif tedavisi; nötrofil lenfosit oranı.

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