

# The Efficacy of Blood Parameters and Its Derivatives in the Diagnosis of Acute Cholecystitis

## Akut Kolesistit Tanısında Kan Parametreleri ve Türevlerinin Tanı Koymadaki Etkinliği

Levent ŞAHİN<sup>1</sup>, Hüseyin Fatih GÜL<sup>2</sup>, Turgut DOLANBAY<sup>1</sup>, Mustafa MAKAV<sup>3</sup>, Murat ARAS<sup>1</sup>

<sup>1</sup>Kafkas University, School of Medicine, Health Practice and Research Hospital, Emergency Medicine Department, Kars

<sup>2</sup>Kafkas University, School of Medicine, Medical Biochemistry, Kars

<sup>3</sup>Kafkas University, School of Veterinary Medicine, Physiology, Kars

### Abstract

The aims of our study are to evaluate the demographic data of patients admitted to the emergency room with acute cholecystitis and determine the sensitivity and specificity of various infection parameters and ratios, primarily the neutrophil lymphocyte ratio (NEU/LYM), in diagnosis. 59 patients diagnosed with acute cholecystitis (the cholecystitis group) and 66 patients not diagnosed with acute cholecystitis (the control group) were viewed. Both groups were admitted to the emergency room with abdominal pain. The demographic data of the patients such as age, gender, complaints during their admission, and their laboratory parameters were recorded on their forms and their statistical analyses were conducted. There were 22 (37.3%) female patients and 37 (62.7%) male patients in the cholecystitis group. Considering the age distribution, 30.5% of the total patient group was over the age of 65. When the admission complaints were evaluated, the most frequent complaint (92.2%) was abdominal pain. The increase in white blood cells (WBC), NEU, c-reactive proteins (CRP), NEU/LYM, WBC/mean platelet volume (MPV) levels and decrease in WBC/NEU levels in the control group were found to be statistically significant ( $p<0.05$ ). As a result of comparing the cholecystitis group with the control group, a ROC analysis was conducted and the cut-off values were determined as; WBC:  $7.25 \times 10^3/\mu\text{L}$ , lymphocyte:  $2.07 \times 10^3$  cells/ $\mu\text{L}$ , neutrophil:  $4.5 \times 10^3/\mu\text{L}$ , CRP: 0.17 mg/L, WBC/NEU: 1.62, NEU/LYM: 2.06, WBC/MPV: 0.873 and CRP/LYM: 0.06. We think that WBC, neutrophil, CRP, NEU/LYM, WBC/MPV and CRP/LYM ratios in acute cholecystitis, can be beneficial in clinical use in terms of the diagnosis.

**Keywords:** Cholecystitis, C-reactive Protein, Emergency, Neutrophil Lymphocyte Ratio

### Introduction

When all of the patients admitted to the emergency room were examined, it was seen that the number of admissions with abdominal pain was quite high. Acute cholecystitis, which is one of the most important and frequent causes of abdominal pain, is a disease that results from the obstruction of

### Öz

Çalışmadaki amaçlarımız, akut kolesistitli hastaların demografik verilerini değerlendirmek ve nötrofil lenfosit oranı (NEU/LYM) başta olmak üzere çeşitli enfeksiyon parametreleri ve oranlarının tanı koymadaki sensitivite ve spesifite oranlarını belirlemektir. Karın ağrısı şikayeti ile acil servise başvuran akut kolesistit tanısı konulan (kolesistit grubu) 59 hasta ile akut kolesistit tanısı olmayan karın ağrısı şikayeti ile gelen (kontrol grubu) 66 hasta incelendi. Hastaların yaş, cinsiyet, başvuru anındaki şikayetleri gibi demografik verileri ve laboratuvar parametreleri çalışma formlarına kayıt edildi ve istatistiksel analizleri yapıldı. Kolesistit grubunda 22 (%37.3) kadın hasta, 37 (%62.7) erkek hasta vardı. Yaş dağılımına bakıldığında bakıldığında toplam hasta grubunun %30.5'i 65 yaş üstü hastalardı. Başvuru şikayetlerine göre değerlendirildiğinde en sık karın ağrısı (%92.2) şikayeti vardı. Kontrol grubunda white blood cell (WBC), NEU, c-reaktif protein (CRP), NEU/LYM, WBC/mean platelet volume (MPV) oranı ve CRP/LYM oranı değerlerindeki artış ve WBC/NEU değerindeki düşüş istatistik açıdan anlamlı bulundu ( $p<0.05$ ). Kolesistit grubunun, kontrol grubuyla karşılaştırılması sonucu ROC analizi yapılmış ve cut off değerleri; WBC:  $7.25 \times 10^3/\mu\text{L}$ , lenfosit:  $2.07 \times 10^3$  cells/ $\mu\text{L}$ , nötrofil:  $4.5 \times 10^3/\mu\text{L}$ , CRP: 0.17 mg/L, WBC/NEU: 1.62, NEU/LYM: 2.06, WBC/MPV: 0.873 ve CRP/LYM: 0.06 olarak tespit edilmiştir. Akut kolesistitte WBC, nötrofil, CRP, NEU / LYM, WBC / MPV ve CRP / LYM oranlarının klinik kullanımda tanı açısından faydalı olabileceğini düşünüyoruz.

**Anahtar Kelimeler:** Acil, C-reaktif Protein, Kolesistit, Nötrofil Lenfosit Oranı

the cystic duct, commonly with a gallstone (95%), and ends with the inflammation and distension of the gallbladder (1). The gallbladder and biliary tracts being obstructed because of gallstones is one of the most commonly seen biliary system emergencies (2). When the patients with cholelithiasis were examined, the presence of cholecystitis was observed in approximately 20% of them (3). While its etiology remains partially unknown, cholecystitis is more frequently seen in cases such as burns, major trauma, sepsis, diabetes mellitus (DM), organ failure, major surgical intervention and vasculitis (4). When the clinical results of patients with acute cholecystitis are examined, nausea, vomiting, and upper right quadrant ache are frequently observed. Ultrasonography (USG) is the primary imaging method used in the evaluation of gallbladder pathologies. Contrast computer tomography (CT) is also used for differential diagnosis in diagnosis and staging (5).

	ORCID No
Levent ŞAHİN	0000-0003-0193-4393
Hüseyin Fatih GÜL	0000-0002-9828-1298
Turgut DOLANBAY	0000-0002-4092-1192
Mustafa MAKAV	0000-0003-1879-8180
Murat ARAS	0000-0002-4329-4147

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Adres / Correspondence : Levent ŞAHİN  
Kafkas University, School of Medicine, Health Practice and Research Hospital, Emergency Medicine Department, Kars

e-posta / e-mail : levsahin44@gmail.com

In addition to imaging methods that have a place in the diagnosis of acute cholecystitis such as CT and USG, many biochemical blood tests and derivative blood parameters derived from them are utilized since they are cheap and give quick results. It is known that especially WBC, CRP and MPV from the biochemical blood parameters are efficient and useful indicators in the laboratory diagnosis of acute cholecystitis (6).

In clinics, the neutrophil (NEU) and lymphocyte (LYM) ratio is a derived blood parameter easily obtained with the ratio of the two parameters detected with a complete blood cell count and are indicators of inflammation. When recent studies are reviewed, although they are shown as prospective indicators for the diagnosis of various diseases, particularly DM, appendicitis, coronary heart diseases, there is not a lot of information about the diagnostics of these derived parameters in the preliminary diagnosis of acute cholecystitis yet (7,8).

The aims of the present study are to examine the demographic data of patients who were admitted to the emergency room and were diagnosed with acute cholecystitis, and investigate the efficacy of values such as WBC, LYM, CRP, CRP/LYM, WBC/NEU, NEU/LYM and WBC/MPV ratio in diagnosis.

## Material and Method

The ethics committee approval for our study was received from Kafkas University Medical Faculty Ethics Committee with the decision dated 30.10.2019 and numbered 80576354-050-99/235. The data of 125 patients over the age of 18 admitted to the emergency room with abdominal pain and diagnosed with cholecystitis during the last 1-year period (between 01.11.2018-01.11.2019) were collected from the hospital automation system and patient files and they were examined retrospectively. All patients who had abdominal pain due to post-trauma, cancer, metastases, endocrine and metabolic diseases, patients whose data were not completely accessible and the patients who were under the age of 18 were excluded from the study. According to the abdominal USG and/or abdomen CT results of the 125 patients who were included in the study, patients were divided into two groups; 59 patients having acute cholecystitis as group 1, 66 healthy patients not having acute cholecystitis or abdominal pain secondary to an infection as group 2. While the age and gender from the demographic features of the cholecystitis and control group were being evaluated, the average WBC, NEU, LYM levels from the complete blood parameters and CRP levels from routine biochemical markers were examined in addition to their derivatives, NEU/LYM, WBC/NEU, WBC/MPV and CRP/LYM ratios. Since all patients were included

in the study, it was not found necessary to conduct a power analysis.

The data obtained in the study were analyzed using the statistics program Statistical Package for Social Sciences (SPSS) version 22.0 (SPSS Inc., Chicago, IL, USA). The data that fit the normal distribution was determined as average  $\pm$  standard deviation. The difference between groups was analyzed by conducting the Student's t-test between the control group and the cholecystitis group. Correlation analysis was used to evaluate the relationship between WBC, neutrophil, CRP, WBC/NEU, NEU/LYM, WBC/MPV and CRP/LYM ratios. Blood parameters and the cut-off values of their ratios were calculated for the ROC analysis. Then, for each of the blood parameters of group 1 with 59 patients and group 2 with 66 patients, a wide range of analyses about the estimated value of each tested parameter were carried out using the ROC curve extracted from the receiver operating characteristic curve AUC the area that falls under the ROC curve.

A graph was drawn for each analyzed result for every value (WBC, lymphocyte, neutrophil, CRP, WBC/NEU, NEU/LYM, WBC/MPV and CRP/LYM), thus a ROC curve was created. In the ROC curve analysis, the sensitivities, specificities, AUC values were analyzed. The value  $p < 0.05$  was accepted as significant in all statistical analyses.

## Results

When 436 patients who referred to our clinic with abdominal pain were examined one by one, it was seen that of 59 patients were diagnosed with cholecystitis, 22 of them (37.3%) were female, 37 (62.7%) of them were male. When the age distribution of the patients was examined, it was found that 30.5% of the total patient group consisted of patients over the age of 65. As for the control group, there were 26 males and 40 females. When the patients were evaluated according to the admission complaints, it was observed that the most common complaint was abdominal pain (92.2%). It was followed by nausea and vomiting (42.3%). In approximately 30% of the patients, there was more than one complaint during the admission. There were 2 patients who had abdominal pain, nausea-vomiting and fever complaints together. The laboratory parameters of the cholecystitis group and the control group were examined.

While the average blood parameter and ratio values in the cholecystitis group were respectively found as; WBC:  $9.54 \pm 3.54 \cdot 10^3/\mu\text{L}$ , lymphocyte:  $2.27 \pm 3.55 \cdot 10^3$  cells/uL, neutrophil:  $7.91 \pm 8.05 \cdot 10^3/\mu\text{L}$ , CRP:  $3.31 \pm 5.03$  mg/L, WBC/NEU:  $1.44 \pm 0.35$ , NEU/LYM:  $5.12 \pm 4.54$ , WBC/MPV:  $1.13 \pm 0.46$  and CRP/LYM:  $2.97 \pm 5.53$ . These values for the control group were respectively found as; WBC:  $7.19 \pm 1.68 \cdot 10^3/\mu\text{L}$ , lymphocyte:

4.59±19.33  $10^3$  cells/uL, neutrophil: 4.44±1.32  $10^3/\mu\text{l}$ , CRP: 0.15±0.11 mg/L, WBC/NEU: 1.66±0.25, NEU/LYM: 2.29±1.12, WBC/MPV: 0.84±0.22 and CRP/LYM: 0.08±0.08 (Table 1). When the control group and the cholecystitis group was compared, the increase in WBC, NEU, CRP,

NEU/LYM, CRP/LYM values in the cholecystitis group and the decrease in the WBC/NEU value were found to be statistically significant ( $p<0.05$ ) (Table 1).

**Table 1.** The average values and p values of blood parameters and their derivations in the control group and cholecystitis group

Blood parameters and Ratios	Groups	Average and Standard deviation	P value
WBC ( $10^3/\mu\text{l}$ )	Control	7.19 ± 1.68	0.000
	Cholecystitis	9.54 ± 3.54	
LYM ( $10^3$ cells/uL)	Control	4.59 ± 19.33	0.367
	Cholecystitis	2.27 ± 3.55	
NEU ( $10^3/\mu\text{l}$ )	Control	4.44 ± 1.32	0.002
	Cholecystitis	7.91 ± 8.05	
CRP (mg/L)	Control	0.15 ± 0.11	0.000
	Cholecystitis	3.31 ± 5.03	
WBC/NEU	Control	1.66 ± 0.25	0.000
	Cholecystitis	1.44 ± 0.35	
NEU/LYM	Control	2.29 ± 1.12	0.000
	Cholecystitis	5.12 ± 4.54	
CRP/LYM	Control	0.08 ± 0.08	0.000
	Cholecystitis	2.97 ± 5.53	
WBC/MPV	Control	0.84 ± 0.22	0.000
	Cholecystitis	1.13 ± 0.46	

The data from the WBC, CRP, NEU, WBC/NEU, NEU/LYM, WBC/MPV and CRP/LYM ratios were found to be statistically significant ( $p<0.05$ ). In the cholecystitis group; a statistically significant positive correlation between the LYM and WBC values was observed when the NEU values were examined. A statistically significant negative correlation between the patients' WBC/NEU ratio and WBC, LYM, NEU was observed. A statistically significant positive correlation was observed between the MPV, CRP and NEU/LYM ratios when the patients' CRP/LYM ratio was examined. A negative correlation between patients' WBC/MPV ratio and MPV and WBC/NEU, a statistically significant positive correlation between NEU and WBC was found. A negative correlation between NEU/LYM and WBC/NEU, a statistically significant positive correlation between CRP and the WBC/MPV ratio was observed.

As a result of comparing the cholecystitis group with the control group, ROC analysis was conducted and the cut-off values were determined as WBC: 7.25  $10^3/\mu\text{l}$ , lymphocyte: 2.07  $10^3$  cells/uL, neutrophil: 4.5  $10^3/\mu\text{l}$ , CRP: 0.17 mg/L, WBC/NEU: 1.62, NEU/LYM: 2.06, WBC/MPV: 0.87 and CRP/LYM: 0.06 (Figure 1).

Both sensitivity and specificity values were taken into consideration while conducting the ROC analysis. In the ROC analysis, sensitivity, specificity, 95% confidence interval for sensitivity, 95% confidence interval for specificity, cut-off values and AUC values were examined for the blood parameters and ratios. CRP was found to be

the highest in sensitivity (89.83%) and specificity (69.70%) (Table 2). While LYM was found to be the lowest in sensitivity (64.41%), WBC and WBC/MPV were the lowest in specificity (50.00%).

## Discussion

When the cholecystitis cases were examined according to the age and gender, cholecystitis was most frequently found between the ages 30-60 and in women (3). The age of occurrence in our study was consistent with the literature. We attribute the reason for a higher number of male patients, unlike the literature, to a habit of eating out a lot and irregular eating habits in terms of meat and fats.

It was found that approximately 5-10% of the patients admitted to the emergency room with the complaint of abdominal pain were patients diagnosed with acute cholecystitis (9). In our study, when all of the abdominal pain cases ( $n=436$ ) determined as the reference in our study were examined, the ratio of patients diagnosed with acute cholecystitis was 7.39%, consistent with the literature.

Cholecystitis, which occurs as a result of inflammation in the gallbladder, has some systemic symptoms; these are high fever, CRP and WBC. CRP is an acute phase reactant frequently used in clinical practice. It is found in high levels in many infectious, autoimmunity and neoplastic diseases, including acute cholecystitis. Similar to our study, in the Bedel's study, when the cholecystitis group was compared to the control group the WBC, CRP,

NEU/LYM values of the cholecystitis group were found to be significantly higher than those of control group ( $p<0.001$ ) (10).

In another study conducted about the patients with acute cholecystitis, it was argued that high NEU/LYM can be used in diagnosis. In this Lee's study, the patients were evaluated separately as under the age of 50 and over the age of 50, and it was observed that the patients over the age of 50 had higher NEU/LYM (11). Also, it has been suggested in another study that having NEU/LYM results as  $\geq 3$  is an indicator of the disease's severity. NEU/LYM can be easily calculated with routine blood tests from patients. However the

determined value for the diagnosis of acute cholecystitis has not been revealed yet (12).

In Başol's study, the mean NEU/LYM was determined as  $5.37\pm 4.9$ , and the NEU/LYM value was found to show no significant difference regarding gender and age groups ( $p>0.05$ ) (13). In Beliaev's study, they found the WBC number as  $12.2 \cdot 10^3/\mu\text{l}$  on average, NEU/LYM as 8.5 on average (14). It was WBC:  $9.54\pm 3.54 \cdot 10^3/\mu\text{l}$ , NEU/LYM:  $5.12\pm 4.54$  in our study. It was determined as high in proportion with the infection and can be considered to use as an inflammatory marker.

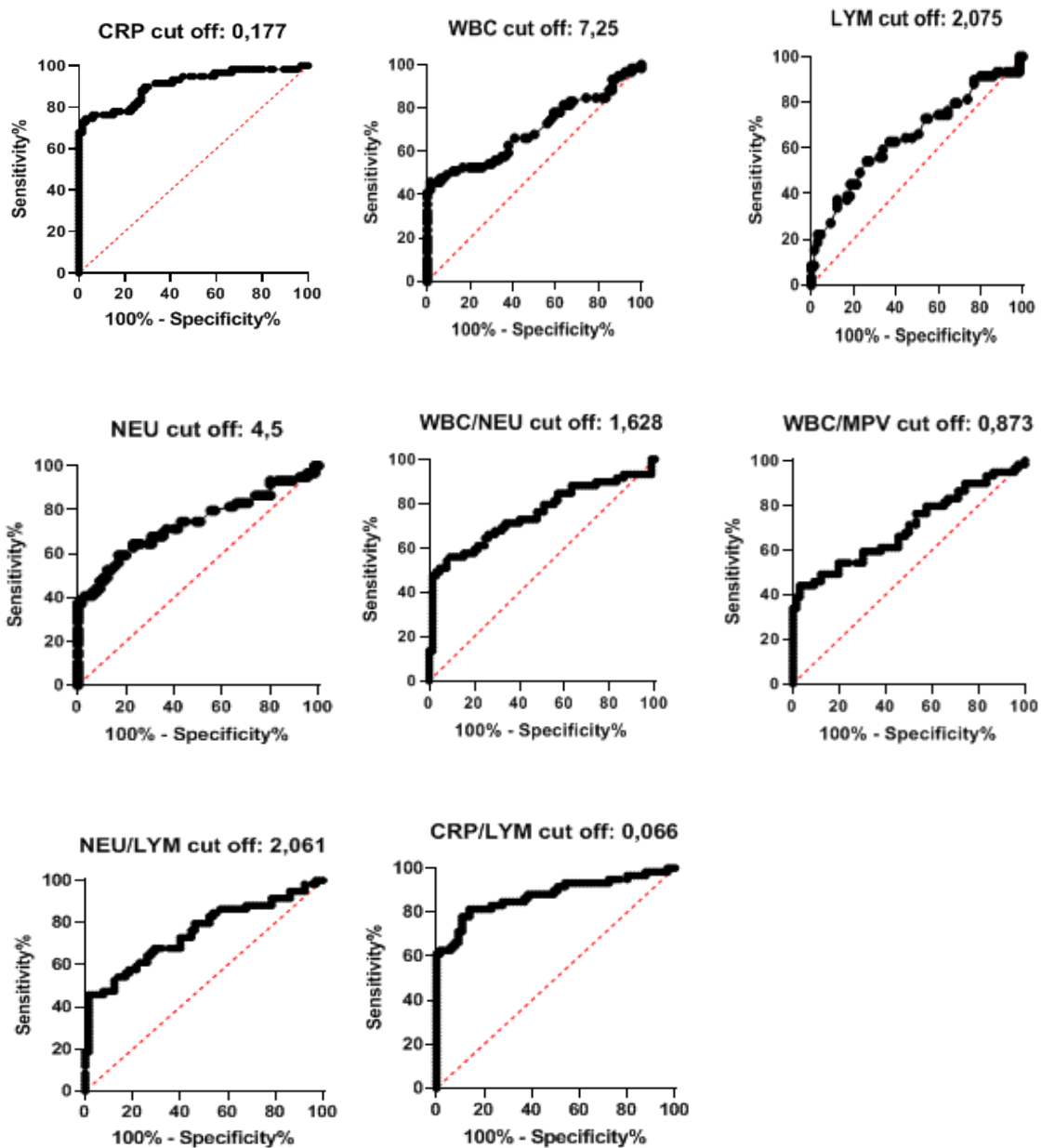


Figure 1. The ROC curve for the values of blood parameters and its derivatives

**Table 2.** Sensitivity, specificity and AUC values of blood parameters and ratios used in ROC analysis in cholecystitis patients

	WBC	NEU	LYM	CRP	WBC/NEU	NEU/LYM	WBC/MPV	CRP/LYM
<b>Sensitivity</b>	67.80%	71.19%	64.41%	89.83%	72.88%	74.58%	69.49%	88.14%
<b>SN, 95% CI</b>	55.11-78.31	58.62- 81.16	51.66-75.40	79.54- 95.26	60.40- 82.56	62.20- 83.94	56.85-79.75	77.48- 94.13
<b>Specificity</b>	50.00%	58.46%	52.31%	69.70%	52.31%	55.38%	50.00%	61.54%
<b>SP, 95% CI</b>	38.27-61.73	46.34-69.64	40.38-63.98	57.78- 79.45	40.38- 63.98	43.34- 66.83	38.27-61.73	49.38- 72.40
<b>AUC</b>	0.698	0.736	0.652	0.906	0.752	0.751	0.7013	0.876
<b>AUC, 95% CI</b>	0.603- 0.794	0.646-0.827	0.554-0.749	0.852-0.960	0.663-0.842	0.664- 0.839	0.607-0.795	0.810- 0.941
<b>Cut-off</b>	7.250	4.500	2.075	0.170	1.628	2.061	0.873	0.066

In a study conducted about the hemogram parameter levels in acute cholecystitis, the average LYM number was found as  $1.5 \pm 1.15$  K/uL  $10^3/\text{mm}^3$  when the blood count results of the patients were examined (15). These values were consistent with the literature in our study.

In a study conducted on CRP levels in patients diagnosed with acute cholecystitis, the CRP level was calculated as  $6.79 \pm 1.25$  mg/L (16). On the other hand, it was determined that the CRP levels in our study were higher than the normal reference range.

In Cardall's study, the sensitivity of the WBC number was found as 76% and its specificity was found as 52% in the diagnosis of acute cholecystitis, and clinicians were suggested not to use this parameter as an indicator in the diagnosis (17). In our study, the sensitivity for WBC in acute cholecystitis patients was found as 67.80%, while the specificity was observed to be consistent with this study (50%).

In Bedel's study, for the laboratory parameters in the diagnosis of acute cholecystitis, the sensitivity, specificity and AUC values for WBC, with the cut-off value accepted as 8.95, was found as 66.4%, 72.8% and 0.716%, respectively. For CRP, whose cut-off value was accepted as 9.5, sensitivity, specificity and AUC values were found as 70%, 73.2% and 0.716% respectively. In our study, when the ROC analysis was conducted by comparing the result of cholecystitis group with the control group, the sensitivity and AUC value for WBC was found to be similar to the results of the study carried out by Bedel's study, while the specificity percentage was found to be lower (50%). On the other hand, the specificity percentage for CRP was found to be consistent with the literature (10).

In a study, where a ROC analysis for NEU/LYM with a cut-off value of 6.56 was conducted, the sensitivity was found as 77.5%, specificity as 67.5% and AUC value as 0.736 in the cholecystitis group (18). In our study, while the sensitivity and AUC values showed similarities, specificity was found to be lower.

When a literature review was carried out for the CRP/LYM ratio, the ROC analysis results for acute cholecystitis could not be obtained. In acute cholecystitis patients, it was found as high CRP/LYM sensitivity (88.14%) and specificity

(61.54%) in the ROC analysis evaluation in our study. We believe that this study can give a parameter since ratios not available in the literature and shed light for the studies to be conducted about this topic.

In conclusion; currently many indicators are being used to diagnose acute cholecystitis. Especially during the first stage of evaluating the patient, examining hemogram and biochemical blood tests accelerates the diagnosis process since it is cheaper, easier and more accessible compared to imaging methods. In the blood tests that are given to patients, who refer to the emergency room, the WBC, NEU, CRP, NEU/LYM, CRP/LYM, WBC/NEU and WBC/MPV ratio can be beneficial in clinical use for the diagnosis. It is necessary that the indicators in the study are analyzed in a more comprehensive sample.

**Ethics Committee Approval:** The ethics committee approval for this study was received from Kafkas University Medical Faculty with the decision dated 30.10.2019 and numbered 80576354-050-99/235.

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