DOI: 10.14744/cm.2023.18209
Comprehensive Medicine 2023;15(2):125-131

RESEARCH ARTICLE

Diagnostic Value of the Systemic Immune-Inflammation Index in Diagnosing Acute Cholecystitis

Kemal Şener[1], Adem Çakır[1], Hüseyin Kılavuz[2], Serkan Doğan[3], Ramazan Güven[1], Semih Korkut[1]

[1]Department of Emergence Medicine, Republic of Türkiye, Ministry of Healthy Başaksehir Çam and Sakura State Hospital, İstanbul, Türkiye
[2]Department of General Surgery, Republic of Türkiye, Ministry of Healthy Başaksehir Çam and Sakura State Hospital, İstanbul, Türkiye
[3]Department of Emergence Medicine, Kanuni Sultan Süleyman Training and Research Hospital, İstanbul, Türkiye

ABSTRACT

Objective: Acute cholecystitis (AC) is an acute inflammatory disease of the gallbladder. Although there are algorithms used today in the diagnosis of AC, there is still a need for inexpensive and fast diagnostic parameters. The systemic immune-inflammation index (SIII) is a novel prognostic indicator of systemic inflammation. In our study, the prognostic value of SIII in the differential diagnosis of AC was investigated.

Materials and Methods: Our study was designed as a retrospective single-center study. The study was conducted with 150 patients who were admitted to the emergency department with abdominal pain and diagnosed with AC and a control group of 150 patients not diagnosed with AC.

Results: In our results, the white blood cell, neutrophil, and C-reactive protein mean values were found to be statistically significantly higher in the study group than in the control group. Once the cutoff value was established at 743.92 (×109 /dL), the SII was found to have a sensitivity of 70% and a specificity of 59.2% in the diagnosis of AC. This assessment was also performed for neutrophil-to-lymphocyte ratio, and with a cutoff value of 2.91, it had a sensitivity of 62% and a specificity of 61.3%. There was no significant relationship between the Gangrenous cholecystitis (GC) and non-GC groups in terms of the diagnostic value of SIII.

Conclusion: The present study found that the SIII is an index that can be used in the diagnosis of AC but be unsuccessful in distinguishing between GC and non-GC types.

Keywords: Acute cholecystitis, gangrenous cholecystitis, neutrophil-to-lymphocyte ratio, systemic immune-inflammation index

How to cite this article: Şener K, Çakır A, Kılavuz H, Doğan S, Güven R, Korkut S. Diagnostic Value of the Systemic Immune-Inflammation Index in Diagnosing Acute Cholecystitis. CM 2023;15(2):125-131

INTRODUCTION

Acute cholecystitis (AC) is a disease caused by inflammation of the gallbladder. AC is responsible for 3–10% of the etiology of abdominal pain. It usually occurs as a result of bile duct obstruction.[1–3] Gallbladder stones are formed due to the high carbohydrate and fatty diet, which is especially common in Western societies, and clinical conditions such as cholecystitis occur as a result of their blockage of the cystic duct. As a result of this obstruction, edema of the gallbladder wall and subsequently wall ischemia due to edema develops. This condition is called gangrenous cholecystitis (GC). GC is a poorly progressive complication of AC and usually results from a delay after the onset of symptoms.[4]

Detailed anamnesis and systemic physical examination are of great importance in the diagnosis of AC. Imaging methods such as complete blood count (CBC), biochemical parameters, C reactive protein (CRP), erythrocyte sedimentation rate values and ultrasonography, and abdominal computed tomography can also be used to support the diagnosis.[1] And also, ratios such as neutrophil-lymphocyte ratio (NLR), platelet-lymphocyte ratio (PLR), and mean platelet volume obtained from CBC have also been shown to be used in the diagnosis of AC.[5] However, new parameters with high sensitivity and selectivity are still needed in the diagnosis of AC.

The systemic immune inflammation index (SIII) is a prognostic indicator of systemic inflammation that has been associated with outcomes in patients with malignancy as well

Address for Correspondence: Kemal Şener, Department of Emergence Medicine, Republic of Türkiye, Ministry of Healthy Başaksehir Çam and Sakura State Hospital, İstanbul, Türkiye
E-mail: drkemalsener@hotmail.com **ORCID ID:** 0000-0002-8579-6663

Received date: 13.02.2023
Revised date: 20.02.2023
Accepted date: 23.02.2023
Online date: 21.03.2023

as acute and chronic inflammation-related diseases.[6] We think that SIII will help to obtain more accurate results in the diagnosis of AC since it is a cheap parameter that requires CBC parameters, does not contain subjective findings, can be easily calculated, and is inexpensive.

MATERIALS and METHODS

Study Setting

This study started after obtaining the study approval from the ethics committee of our hospital (Ethics committee date: April 28, 2021 and ethics committee decision no: 2021.04.35). Our study was designed as a retrospective and single-center study.

Of the patients who were admitted to the emergency department with abdominal pain and were diagnosed with AC between May 01, 2021, and June 15, 2022, those who met the inclusion criteria were included in the present study. Demographic data, medical history, leukocyte count white blood count (WBC), thrombocyte count, neutrophil count, SIII, CRP, vital signs, presence of GC, and pathology results of the samples from cholecystectomy were obtained from the Hospital Information Management System and the data retrieved from the system were then saved on the case form. AC cases were divided into two groups as GC and non-GC. The study included 150 cases with confirmed AC and 150 patients who were admitted to the emergency department with abdominal pain and were not diagnosed with AC.

Study Population

Adult patients who presented to the emergency department with abdominal pain and whose diagnosis of AC were confirmed as a result of the evaluation and whose data were not missing were included in the study, and these patients constituted the study group. Cases with abdominal pain who were not diagnosed with AC formed the control group. Patients under the age of 18, pregnant women, cases with missing data, cases whose outcomes could not be followed up, cases with unknown histories, cases with a history of any malignancy or hematological disease, cases with bone marrow pathology, and cases with a history of anti-inflammatory or immunosuppressive drug use were excluded from the study. In addition, cases with non-AC infection focus were not included in the study.

Data Collection

To identify the patients to be included in the study, the hospital's information management system was used to access the patient files. To detect AC, the ICD10 diagnostic codes "K81, K81.0, K81.8, and K81.9" were used on the hospital's information management system. Consequently, 208 patients were identified. Of the 208 cases identified, 19 were excluded because they had a history of malignancy, 11 were excluded due to missing data, seven were excluded because they had a history of hematological disease, and one was excluded due to pregnancy. The remaining 170 cases were listed in the order of date and time of admission, and the first 150 patients were included in the study.

Study Group

208 cases	
189 cases had no history of malignancy	19 cases had a history of malignancy
↓	
189 cases	
178 cases had no missing data	11 cases had missing data
↓	
178 cases	
171 cases had no history of hematological disease	7 cases had a history of hematological disease
↓	
171 cases	
170 cases were not pregnant	There is pregnancy in 1 case
↓	
170 Cases Remaining	

In our study, the patients recruited for the study group were selected based on the gold standard pathology results.

The control group was formed randomly in accordance with the inclusion and exclusion criteria and in compliance with the mean age of the patients. The control group included 150 patients who were admitted with the complaint of "abdominal pain" but were not diagnosed with AC in their patient evaluation. These patients were volunteers with a known medical history and no history of chronic disease.

Data Calculation

In the study, calculations were made using the hemogram results obtained for each case. P, N, and L refer to peripheral platelet, neutrophil, and lymphocyte counts, respectively. Accordingly, NLR (N/L Ratio), PLR (P/L Ratio), and SIII ((P x N)/L ratio) were calculated.

Statistical Analysis

Descriptive data were presented as number (n), percentage (%), mean value, and standard deviation. Kolmogorov–Smirnov test was used to evaluate the distribution of data.

Table 1. Comparison of the demographic and clinical data of the patient and control groups

Parameter	Patient group (n=150)			Control group (n=150)			p
	n	%	Mean±SD	n	%	Mean±SD	
Demographic data							
Male	59	39.3		69	46.0		0.243[p]
Age (years)			47.53±16.31			44.43±18.91	0.130[t]
Laboratory tests							
WBC (×10^9/L)			10.31±4.04			8.71±2.90	**<0.001[t]**
Neutrophil (×10^9/L)			7.50±3.77			5.80±2.66	**<0.001[t]**
Lymphocyte (×10^9/L)			1.93±1.01			2.06±1.04	0.279[t]
Platelet (×10^9/L)			294.52±235.07			255.68±65.60	0.052[t]
CRP (mg/dL)			35.37±61.11			21.00±40.77	**0.017[t]**
Ratios							
NLR			5.28±4.68			4.10±4.84	**0.034[t]**
PLR			189.75±130.44			157.42±112.77	**0.022[t]**
SIII			1459.91±1310.56			980.64±10.31	**0.001[t]**

[t]: Independent T-test; [p]: Pearson χ^2 test. SD: standard deviation; WBC: White blood cell; CRP: C-reaktif protein; NLR: Neutrophil-lymphocyte ratio; PLR: Platelet lymphocyte ratio; SIII: Systemic immune-inflammatory index

Pearson χ^2 test was used to compare categorical data and Fisher's Exact test was used to compare less than 5 data. Independent t-test was used to compare two independent numerical values. ROC curve analysis was performed to evaluate the diagnostic power of the parameters and indices used in AC cases and to determine the correlation of these values with GC and non-GC.

P<0.05 was considered statistically significant.

RESULTS

One hundred and fifty patients and 150 controls were recruited for the present study. A randomized control group was formed in a way ensuring that the groups are of similar ages and have similar gender distributions. The control group included patients without comorbid disease. Therefore, the study does not present a comorbidity-based comparison. Of the laboratory values, the WBC, neutrophil, and CPR mean values were found to be statistically significantly higher in the study group than in the control group.

The SIII, NLR, and PLR values calculated with the patient data obtained in the study and control groups were compared, and the SIII, NLR, and PLR values were found to be significantly higher in the patient group (Table 1).

Based on the evaluation of the cases in the patient group, 132 cases were non-GC and 18 had GC. There was no significant difference between the groups of GC and non-GC cases in terms of age and gender. The incidence of diabetes mellitus in the group of GC cases was significantly higher than in the non-GC group, while there was no significant difference between these two groups in terms of incidence of other comorbid diseases. In terms of vital parameters, it was observed that the two groups had similar mean values in systolic blood pressure, diastolic blood pressure, pulse, and fever (Table 2).

The mean level of WBC was found to be significantly higher in the GC group than in the non-GC group, while there was no significant difference between these two groups in terms of neutrophil, lymphocyte, platelet, and CRP levels. We also found that there was no significant difference between the two groups in terms of SIII, NLR, and PLR values that were calculated using the aforementioned data.

To assess the diagnostic value of SIII and NLR parameters in AC cases, their sensitivity and specificity were also studied based on the respective cutoff values. In this evaluation, with the cutoff value set at 743.92 (x10^9/dL), SIII had 70% sensitivity and 59.2% specificity in the diagnosis of AC. This evaluation was also performed for NLR and, with the cutoff

Table 2. Comparison of the data of the gangrenous and non-gangrenous cholecystitis cases

Parameter	Gangrenous Cholecystitis (n=18)			Non-Gangrenous Cholecystitis (n=132)			p
	n	%	Mean±SD	n	%	Mean±SD	
Demographic data							
Male	10	55.6		49	37.1		0.133[p]
Age (years)			51.61±9.98			46.98±16.94	0.260[t]
Comorbid diseases							
Hypertension	5	27.8		39	29.5		0.877[p]
Diabetes mellitus	15	83.3		28	21.2		**<0.001[p]**
Coronary artery disease	1	5.6		9	6.8		0.840[f]
Laboratory tests							
WBC (×10^9/L)			10.66±4.14			7.76±1.82	**0.004[t]**
Neutrophil (×10^9/L)			5.44±4.90			4.06±2.29	0.241[t]
Lymphocyte (×10^9/L)			1.97±1.03			1.64±0.86	0.198[t]
Platelet (×10^9/L)			296.89±248.97			277.11±79.39	0.739[t]
CRP (mg/dL)			37.40±63.85			20.53±32.37	0.273[t]
Ratios							
NLR			5.44±4.90			4.06±2.29	0.241[t]
PLR			193.30±135.59			163.73±81.52	0.369[t]
SIII			1517.99±1368.42			1034.05±637.13	0.142[t]

[t]: Independent T-test; [p]: Pearson χ^2 test; [f]: Fisher's Exact Test. SD: standard deviation; WBC: White blood cell; CRP: C-reaktif protein; NLR: Neutrophil-lymphocyte ratio; PLR: Platelet lymphocyte ratio; SIII: Systemic immune-inflammatory index

value set at 2.91, NLR had a sensitivity of 62% and a specificity of 61.3% (Fig. 1 and Table 3).

DISCUSSION

AC is one of the most common causes of abdominal pain in emergency departments. Emergency medicine clinicians use many methods to diagnose AC. Laboratory parameters and imaging have an important place in the diagnosis of AC. In particular, laboratory values such as WBC, NLR, PLR, PNR or CRP, and cholestasis enzymes level obtained in CBC are used to support the diagnosis. Our study examined the sensitivity of SIII, a parameter that can be measured with CBC, in the diagnosis of AC and whether the SIII is a useful parameter in the differentiation of GC and non-GC cases.

As stated in the literature, NLR is a biomarker for systemic inflammation and stress.[7] In another study conducted with AC patients, Micić et al.[8] found that high NLR, CRP, and WBC values were higher in patients with AC. In a study by Temizi et al.[5] in 2017, the researchers showed that WBC, NLR, and PLR values were higher in patients with AC. Again, in a retrospective cohort study by Beliaev et al.,[9] the power of NLR in diagnosing AC was similar to CRP and stronger than that of WBC. The results of our study are similar to the literature. We found that the mean values of WBC, NLR, PLR, and CRP were higher in the patient group than in the control group. In this context, our results support the results reported in the literature. In addition, we found that the mean SIII value was also significantly higher in the group of AC cases. As far as we know, our study is the first to analyze the diagnostic value of SIII in AC and our results are satisfactory in this regard. However, before jumping to definite conclusions on this issue, it would be beneficial to support the data that we report herein with further studies where higher numbers of patients are included in the study.

The diagnosis of GC poses a diagnostic challenge for clinicians and its pre-operative diagnosis is quite rare. The GC complications are associated with high rates of mortality, and its early diagnosis is critically important.[10] In a study where Real-Noval et al.[11] compared GC and non-GC cases, the mean age in the group of GC cases was 65 and there was no significant difference between the two groups in terms of gender and age. In our study, the mean age was found to be 51.6 years

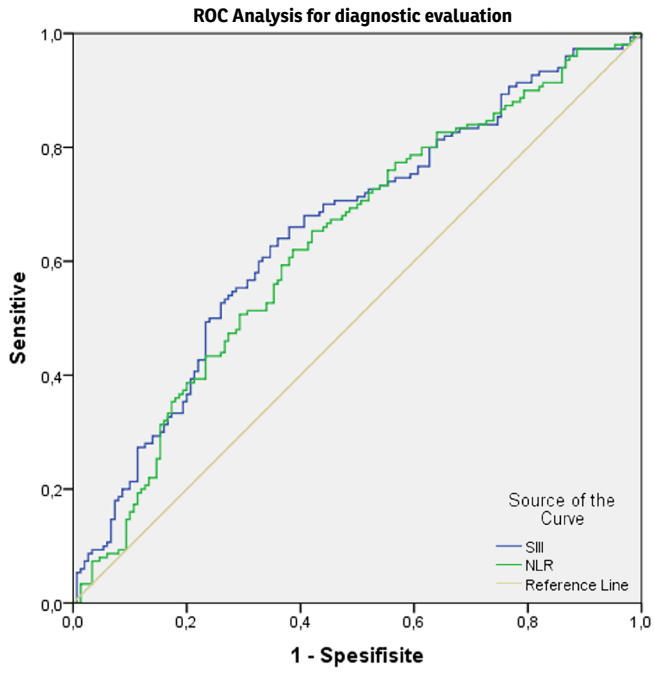

Figure 1. Comparison of SIII and NLR in terms of diagnostic value

ROC: Receiver operating characteristic; SIII: Systemic immune-inflammatory index; NLR: Neutrophil-lymphocyte ratio

and the two groups were similar in terms of age and gender distribution. In this context, the results of our study are different from the literature, and we think that this is due to the population characteristics of the region where we study.

Concerning the relation between chronic diseases and GC, there are studies reporting that diabetes mellitus alone is an independent risk factor for GC.[12,13] In a study by Bourikian et al.,[14] they showed that diabetes and coronary artery disease are risk factors for GC. In addition, in the study of Real-Noval et al.,[11] there was no significant difference between the GC and NGC groups in terms of diabetes mellitus. In our study, we found that the rate of patients with history of diabetes mellitus was significantly higher in the GC group. In this context, the data in our study also support that diabetes mellitus is a risk factor for GC.

In our study, laboratory values of the GC and NGC cases were examined and WBC values were found to be significantly higher in the GC group. In a study by Teefey et al.,[15] the mean WBC was significantly higher in the GC group. Again in the study of Shirah et al.,[13] the GC cases had a significantly higher mean value of WBC than the control group did. In the study of Borzelino et al.,[16] however, it was found that the study groups had similar values of WBC. Although different results are seen in the literature, our study supports the common result that is available in the literature.

Again, in their study, Mok et al.[10] also stated that CRP has a high predictive value in the diagnosis of GC. Mahmood et al.[17] also stated in their study that CPR is one of the independent predictive factors in diagnosing GC. In our study, however, no significant difference was found between the groups in terms of CRP values. We think that this divergence of our results from the data reported in the literature may be due to both the small number of patients included and the initiation of antibiotherapy in AC cases in the early period.

It is seen in the literature that NLR is used in the diagnosis of AC and in determining the risk of GC. In a study by Lee et al.,[7] they stated that NLR values were higher in the GC group. Mahmood et al. and Sato et al.[17,18] both reported that NLR is an independent factor in predicting GC. In the study of Real-Noval et al.,[11] NLR was found to be significantly higher in cases with GC. According to the results from the comparison of the groups of GC and non-GC cases in our study, we did not detect a significant difference in terms of NLR, PLR, and SIII values. We think that this is due to the fact that the cases diagnosed with AC in our hospital can usually be operated on in the early period.

SIII is a marker of inflammatory and immune response used in the evaluation of prognosis, especially in patients

Table 3. Comparison of the ROC analysis results according to the cutoff values of SIII and NLR in the diagnosis of acute cholecystitis

Parameter	AUC	Cutoff value	Sensitivity	Specificity	p	95% CI	
						Lower bound	Upper bound
SIII (×10⁹/dL)	0.653	743.92	70	59.3	<0.001	0.591	0.715
NLR	0.632	2.91	62	61.3	<0.001	0.569	0.695

ROC: Receiver operating characteristic; SIII: Systemic immune-inflammatory index; NLR: Neutrophil-lymphocyte ratio; AUC: Area under curve; CI: Confidence interval

with malignancy. Recently, it has been used in many diseases such as acute coronary syndrome, rheumatoid arthritis, pulmonary embolism, infective endocarditis, and optic neuropathy.[19,20] In our literature review, we did not encounter any article examining the correlation between SIII and AC. We think that SIII is a novel easy-to-calculate and inexpensive biomarker that can be resorted to while diagnosing AC and predicting its prognosis. In a study by Hu et al.[19] on infective endocarditis patients, high SIII values were shown to be helpful in making the diagnosis of infective endocarditis. Again, in a study conducted with ischemic stroke patients, high SIII values were reported to be accurate markers for the diagnosis of stroke.[21]

In our study, we found that SIII had a higher significance in the diagnosis of AC compared to NLR and PLR. In our study, for the diagnostic value that was measured with the cutoff value set at 743.92×10^3/dL, SIII had a sensitivity of 70% and a specificity of 59.2 (AUC: 0.653; %95 CI:0.591–0.715).

CONCLUSION

We found that SIII is a useful index in the diagnosis of AC. The index was, however, found to be unsuccessful in distinguishing between GC and non-GC types. We think that this is due to the small number of patients included and the early initiation of treatment on the patients. However, since our study is the first to measure the diagnostic value of SIII in AC, further studies with larger sample sizes are needed to support our data and strengthen our hypothesis.

None of the authors received any type of financial support that could be considered potential conflicts of interest regarding the manuscript or its submission.

Disclosures

Ethics Committee Approval: The study was approved by the Ministry of Healthy Başaksehir Çam and Sakura State Hospital Clinical Research Ethics Committee (No: 2021.04.35, Date: 28/04/2021).

Informed Consent: Written informed consent was obtained from all patients.

Peer-review: Externally peer reviewed.

Authorship Contributions: Concept: K.Ş., R.G., A.Ç., H.K., S.K., S.D.; Design: K.Ş., R.G., A.Ç., H.K., S.K., S.D.; Supervision: K.Ş., A.Ç., S.D., H.K.; Materials: S.K., A.Ç., K.Ş., R.G.; Data Collection or Processing: S.K., A.Ç., K.Ş., R.G.; Analysis or Interpretation: S.K., A.Ç., K.Ş., R.G.; Literature Search: K.Ş., A.Ç., S.D., H.K.; Writing: K.Ş., A.Ç., S.D., H.K.; Critical review: K.Ş., A.Ç., S.D., H.K.

Conflict of Interest: No conflict of interest was declared by the authors.

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

REFERENCES

1. Burmeister G, Hinz S, Schafmayer C. Acute Cholecystitis. Zentralbl Chir [Article in German] 2018;143:392–9. [CrossRef]
2. Kohga A, Suzuki K, Okumura T, Yamashita K, Isogaki J, Kawabe A, et al. Is postponed laparoscopic cholecystectomy justified for acute cholecystitis appearing early after onset? Asian J Endosc Surg 2019;12:69–73. [CrossRef]
3. Altuğ E. Akut kolesistit ve akut pankreatit. Şener A, Siliv N. Gastrointestinal Sistem Acilleri. Ankara: Akademisyen Kitabevi; 2021. p. 119–34.
4. Jones MW, Genova R, O'Rourke MC. Acute cholecystitis. In: Treasure Island (FL): StatPearls Publishing; 2022. Available at: https://www.ncbi.nlm.nih.gov/books/NBK459171. Accessed Feb 20, 2023.
5. Temizi A, Özdemir Y, Aslan A, Bostancı MT, Atasoy G, Çaparlar MA, et al. Role of complete blood counts parameters in diagnosis of acute cholecystitis. Acta Medica Mediterranea 2017;33:411–6.
6. Chen JH, Zhai ET, Yuan YJ, Wu KM, Xu JB, Peng JJ, et al. Systemic immune-inflammation index for predicting prognosis of colorectal cancer. World J Gastroenterol 2017;23:6261–72. [CrossRef]
7. Lee SK, Lee SC, Park JW, Kim SJ. The utility of the preoperative neutrophil-to-lymphocyte ratio in predicting severe cholecystitis: a retrospective cohort study. BMC Surg 2014;14:100. [CrossRef]
8. Micić D, Stanković S, Lalić N, Đukić V, Polovina S. Prognostic value of preoperative neutrophil-to-lymphocyte ratio for prediction of severe cholecystitis. J Med Biochem 2018;37:121–7.
9. Beliaev AM, Angelo N, Booth M, Bergin C. Evaluation of neutrophil-to-lymphocyte ratio as a potential biomarker for acute cholecystitis. J Surg Res 2017;209:93–101. [CrossRef]
10. Mok KW, Reddy R, Wood F, Turner P, Ward JB, Pursnani KG, et al. Is C-reactive protein a useful adjunct in selecting patients for emergency cholecystectomy by predicting severe/gangrenous cholecystitis? Int J Surg 2014;12:649–53. [CrossRef]
11. Real-Noval H, Fernández-Fernández J, Soler-Dorda G. Predicting factors for the diagnosis of gangrene acute cholecystitis. Cir Cir 2019;87:443–9. [CrossRef]
12. Ripollés T, Martínez-Pérez MJ, Martin G, Vizuete J, Martínez-García R, Diez J, et al. Usefulness of contrast-enhanced US in the diagnosis of acute gangrenous cholecystitis: a comparative study with surgical and pathological findings. Eur J Radiol 2016;85:31–8. [CrossRef]
13. Shirah BH, Shirah HA, Saleem MA, Chughtai MA, Elraghi MA, Shams ME. Predictive factors for gangrene complication in acute calculous cholecystitis. Ann Hepatobiliary Pancreat Surg 2019;23:228–33.
14. Bourikian S, Anand RJ, Aboutanos M, Wolfe LG, Ferrada P. Risk factors for acute gangrenous cholecystitis in emergency general surgery patients. Am J Surg 2015;210:730–3. [CrossRef]
15. Teefey SA, Dahiya N, Middleton WD, Bajaj S, Dahiya N, Ylagan L, et al. Acute cholecystitis: do sonographic findings and WBC count predict gangrenous changes? AJR Am J Roentgenol 2013;200:363–9. [CrossRef]
16. Borzellino G, Steccanella F, Mantovani W, Genna M. Predictive factors for the diagnosis of severe acute cholecystitis in an emergency setting. Surg Endosc 2013;27:3388–95. [CrossRef]
17. Mahmood F, Akingboye A, Malam Y, Thakkar M, Jambulingam P. Complicated acute cholecystitis: the role of c-reactive protein and neu-

trophil-lymphocyte ratio as predictive markers of severity. Cureus 2021;13:e13592. [CrossRef]

18. Sato N, Kinoshita A, Imai N, Akasu T, Yokota T, Iwaku A, et al. Inflammation-based prognostic scores predict disease severity in patients with acute cholecystitis. Eur J Gastroenterol Hepatol 2018;30:484–9.
19. Hu W, Su G, Zhu W, Zhou E, Shuai X. Systematic immune-inflammation index predicts embolic events in infective endocarditis. Int Heart J 2022;63:510–6. [CrossRef]
20. Jiang H, Li D, Xu T, Chen Z, Shan Y, Zhao L, et al. Systemic immune-inflammation index predicts contrast-induced acute kidney injury in patients undergoing coronary angiography: a cross-sectional study. Front Med (Lausanne) 2022;9:841601. [CrossRef]
21. Hou D, Wang C, Luo Y, Ye X, Han X, Feng Y, et al. Systemic immune-inflammation index (SII) but not platelet-albumin-bilirubin (PALBI) grade is associated with severity of acute ischemic stroke (AIS). Int J Neurosci 2021;131:1203–8. [CrossRef]