ORIGINAL ARTICLE

Predictive evaluation of SIRI, SII, PNI, and GPS in cholecystostomy application in patients with acute cholecystitis

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ABSTRACT

BACKGROUND: The aims of this study were to investigate the clinical significance of systemic inflammatory response index (SIRI), systemic inflammation index (SII), prognostic nutritional index (PNI), and Glasgow prognostic score (GPS) in deciding whether to perform cholecystostomy when determining if cholecystostomy is the right choice for acute cholecystitis (AC) patients.

METHODS: Between January 2018 and December 2020, 126 consecutive patients with AC with and without cholecystostomy were retrospectively recruited from the Trakya University in Edirne, Turkey. Group I included AC patients with cholecystostomy and Group II included AC patients without cholecystostomy. The neutrophil/lymphocyte ratio (NLR), platelet/lymphocyte ratio (PLR), and lymphocyte/monocyte ratio (LMR) were calculated. The PNI and SII were calculated

RESULTS: There is significant difference between the two groups by the comparison of SIRI, SII, PNI, and GPS values ($p<0.001$). In Group I, SIRI, SII, and GPS values are higher than the Group II and PNI value in Group I is lower than the Group II. Furthermore, the NLR and PLR ratios in Group I are significantly higher than Group II, and the LMR ratio in Group I is significantly lower than Group II.

CONCLUSION: According to our study, we can say that NLR, PLR, SII, SIRI, and GPS are positive predictors and LMR and PNI are negative predictors for the severity of AC. Therefore, when we decide to treat AC medically, we may prefer the application of cholecystostomy tube at the beginning of hospitalization by the help of evaluating NLR, PLR, LMR, SIRI, SII, GPS, and PNI values.

Keywords: Cholecystitis; cholecystostomy; Glasgow prognostic score; prognostic nutritional index; systemic inflammation index; systemic inflammatory response index.

INTRODUCTION

Acute cholecystitis (AC) is one of the most common reasons for hospitalization in patients of all ages. The early cholecystectomy is the standard treatment for AC, but the disease may be severe and necessitate emergency surgery or other interventions. Within 72 h of the onset of symptoms and before the development of fibrosis, laparoscopic cholecystectomy may be a safe procedure, because the anatomy is usually clear.[1]

However, the morbidity and mortality associated with acute laparoscopic cholecystectomy are high,[2,3] mainly due to anesthetic complications and the presence of serious underlying comorbidities. Therefore, high-risk patients with AC are generally treated through conservative methods including intravenous fluid, antibiotic therapy, and percutaneous cholecystostomy (PC), while surgical intervention is delayed for 6–8 weeks.[4]

To guide the management of patients with AC, the Tokyo Guidelines were developed in 2007 and refined in 2013.[5,6] Patients with Grade I cholecystitis have inflammatory changes in the gallbladder and no associated organ dysfunction. Patients with Grade II AC have leukocytosis, a palpable tender

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mass, and/or marked local inflammation, with no associated organ dysfunction. Patients with Grade III cholecystitis have associated organ dysfunction, including cardiovascular hypotension, neurologic disturbances, respiratory failure, oliguria, hepatic dysfunction, and/or thrombocytopenia.

Delayed presentation and significant comorbid illness are associated with increased morbidity in emergency surgery.[7] Because emergency surgery is poorly tolerated by these patients, the medical team needs to assess the timing of surgery thoroughly. If possible, surgery should be rescheduled as elective. The increased risks of complications of an emergency cholecystectomy can be avoided by the help of PC.

The systemic inflammatory response index (SIRI), which is usually evaluated based on peripheral blood-based parameters, such as lymphocytes, C-reactive protein (CRP), monocytes, neutrophil, or platelet count, has been reported to independently associated with oncologic outcomes in various cancers.[8,9] SIRI is calculated by (N×M)/L (where N, M, and L represent neutrophil counts, monocyte counts, and lymphocyte counts, respectively). Several of these parameters have been converted to ratios, such as the neutrophil-to-lymphocyte ratio (NLR),[10] platelet-to-lymphocyte ratio (PLR),[11] and lymphocyte-to-monocyte ratio (LMR),[12] which have been broadly found to be important prognosis predictors. SIRI is usually associated with the oncologic diseases in many studies, but there has been no study to evaluate the SIRI for the AC.

Systemic immune-inflammation index (SII) is calculated by (N×P)/L (where N, P, and L represent neutrophil counts, platelet counts, and lymphocyte counts, respectively) and is associated with some malignant tumors, such as metastatic renal cell cancer and metastatic castration resistant prostate cancer.[13] Compared with the biomarkers of NLR, LMR, and PLR, the SII may comprehensively reflect the balance between the patient's immunity and the inflammatory condition.

In this study, we aimed to know if SIRI, SII, prognostic nutritional index (PNI), and Glasgow prognostic score (GPS) may be predictive factors for the PC in AC patients who are treated medically due to delayed diagnosis or comorbidities for the emergency cholecystectomy. If there is a relationship between the SIRI-SII and complications during the medical treatment of AC, we can prevent these complications by the help of early PC in these patients.

MATERIALS AND METHODS

Patients

This study was approved by the Ethics Committee of the Trakya University in Edirne, Turkey, and written informed consent was obtained from each participant in accordance with the institutional guidelines. Between January 2018 and December 2020, 126 patients with AC with and without cholecystostomy were retrospectively recruited from the Trakya University in Edirne, Turkey. The criteria for patients being included in this study were being older than 18, having diagnosis of AC 72 h later than the feeling of the abdominal pain, and not having any malignant or hematologic disorders. If the patients were admitted to the hospital within 72 h of their pain starting, surgical treatment was an option. Otherwise, medical treatment became the preferred first choice. Seventy-two hours are important in deciding treatment because after 72 h have passed, surgery is more difficult, and risks of complication are increased during operation and post-operative period. Patients in this study were treated medically due to delayed application to the hospital. There were perforations in 17 patients, but these patients had closed perforations clinic and could be managed by medical treatment by the help of application of cholecystostomy. We divided patients into two groups of 63 patients, according to whether or not they had a cholecystostomy.

Laboratory Tests

Routine laboratory measurements, including white blood cell (WBC) count, neutrophil count, lymphocyte count, monocyte count, platelet count, serum albumin, and CRP were performed before conducting the AC diagnostic interventions or treatments. The NLR, PLR, and LMR were calculated. The PNI was calculated according to the following formula: 10 x serum albumin (g/dl) + 0.005 total lymphocyte count (per mm^3). SII was calculated by the formula: platelet (P) × neutrophil (N)/lymphocyte (L). NLR was calculated by dividing the neutrophil count by the number of lymphocytes. GPS was estimated based on the measurement of CRP and albumin. In patients with CRP values >10 (mg/L), and albumin <35 (g/L), the GPS was accepted as 2, if albumin was ≥35 (g/L) and CRP ≤10 (mg/L), then the GPS was considered as 1. In patients with CRP values >10, if albumin was ≥35 (g/L), then the GPS values were accepted as 1, if albumin was ≥35 (g/L) and CRP ≤10 (mg/L) then the GPS values were accepted as 0, respectively. SIRI was defined as (neutrophil × monocyte)/lymphocyte).

PC

The decision to perform PC was made by a senior surgeon based on a high risk-benefit ratio for AC. The indications for PC in patients with calculus or acalculous cholecystitis were classified into four categories: (1) High risk for surgery due to associated severe comorbidity; (2) severe cholecystitis (not responding to conservative management); (3) patients who refuse cholecystectomy; and (4) suspected empyema of the gallbladder. Patients with gallstone pancreatitis, choledocholithiasis, hepatobiliary or intestinal malignancy, or autoimmune biliary disease, and those younger than 18 were excluded from the study. PC was performed by a specialized interventional radiology team under ultrasound or computed tomography guidance in the interventional radiology unit. The distended gallbladder was visualized and local anesthetic infiltrated into

the skin and subcutaneous tissue. The gallbladder was then cannulated with a plastic pigtail catheter using the Seldinger technique. A small volume of contrast agent was injected and fluoroscopy was used to confirm the position of the catheter and determine the patency of the biliary ductal system. Initial aspirated bile was cultured and antibiotic sensitivity of isolated organisms was established. The catheter was then anchored to the skin.

Statistical Analysis

Normal distribution range was controlled by the Shapiro–Wilk test. The Mann–Whitney U test was used for the variations contrary to the normal distribution range in the comparison of two groups. The relations between qualitative variations were studied by the Pearson Chi-square test and Fisher's accurate test. Median and quarter values have been given for the quantitative variations and percentage and frequency rates were given for the qualitative variations as descriptive statistic evaluation. Significant value was determined as 0.05 for all statistical analysis. Cutoff values for the quantitative variations were also studied by receiver operating characteristic (ROC) analysis. All statistical analyses were performed with the TURCOSA (Turcosa Analytics Ltd Co, Turkey, www.turcosa.com.tr) statistical software program.

Table 1. Comparison of age and gender between Group I and Group II

	Group I	Group II	p-value
Age	70 (63–81)	49 (28–72)	p<0.001
Male	42 (66.7%)	26 (41.2%)	p<0.001
Female	21 (33.3%)	37 (58.8%)	p<0.001

RESULTS

We have two groups in this study. The first group (Group I) includes the patients who were hospitalized for the medical treatment of AC and applied cholecystostomy during the hospital stay due to complications or worsening of clinical situations. The second group (Group II) includes the patients who were internalized for the medical treatment of AC and received successful treatment without any invasive processes. There are 63 patients in each group.

The mean age for the Group I is 70 (63–81) and for the Group II is 49 (28–72) (Table 1). There are 42 (66.7%) male patients in Group I and 26 (41.2%) male patients in Group II (Table 1). Therefore, we can say that older patients and male patients have significant positive predictive value for the complications of AC more than the younger and female patients. There is significant difference between the two groups according to age and gender ratio (p<0.001).

The mean leucocyte (WBC) count for the Group I (15,200/mm^3) is higher than the Group II (9400/mm^3). The mean neutrophil (Neut) count for the Group I (13,600/mm^3) is higher than the Group II (7000/mm^3). The mean NLR for the Group I (11) is higher than the Group II (4.18). The mean PLR for the Group I (233) is higher than the Group II (169.09). The mean CRP value for the Group I (13.3 mg/L) is higher than the Group II (3.7 mg/L). The mean SII value for the Group I (0.17%) is higher than the Group II (0.11%). The mean SIRI value for the Group I (9.1) is higher than the Group II (3.1). There is significant difference between the two groups according to WBC, Neut, NLR, PLR, CRP, SII, and SIRI values (p<0.001) (Table 2).

Table 2. The Comparison of SIRI, SII, and PNI values between two groups

	Group I	Group II	p-value
White blood cell (/mm^3)	15200 (10550–20400)	9400 (7300–12300)	<0.001
Neutrophil (/mm^3)	13600 (8100–17300)	7000 (5000–9300)	<0.001
Neutrophile to lymphocyte ratio	11 (7–19)	4.18 (2.79–7.94)	<0.001
Platelet to lymphocyte ratio	233(158–382)	169.09 (111.11–228.33)	<0.001
C-reactive protein (mg/L)	11.7(7.9–24.9)	2.7 (1.1–7.6)	<0.001
Systemic Inflammatory Index	1100(700–1800)	100 (10–800)	<0.001
Lymphocyte (/mm^3)	1100 (600–1500)	1500 (1100–2100)	<0.001
Lymphocyte to monocyte ratio	1.27 (0.77–2.0)	2.4 (1.38–3.8)	<0.001
Albumin (g/dl)	3.1 (2.8–3.6)	3.8 (3.4–4.2)	<0.001
Prognostic Nutritional Index	31.25 (28.25–36.1)	38.7 (35.3–42.9)	<0.001
Systemic Inflammatory Response Index	9.1 (5.2–18.1)	3.1 (1.7–6.4)	<0.001
Monocyte (/mm^3)	800 (500–1300)	700 (500–900)	0.054
Platelet (x1000/mm^3)	248 (188–309)	259 (214–311)	0.722

SIRI: Systemic Inflammatory Response Index; SII: Systemic Inflammation Index; PNI: Prognostic Nutritional Index.

The mean lymphocyte (Lym) count for the Group I (1100/mm3) is lower than the Group II (1500/mm3). The mean LMR for the Group I (1.27) is lower than the Group II (2.4). The mean albumin (Alb) value for the Group I (3.1g/dl) is lower than the Group II (3.8g/dl). The mean PNI value for the Group I (31.25) is lower than the Group II (38.7). There is significant difference between the two groups according to Lym, LMR, Alb, and PNI values ($p<0.001$) (Table 2).

The mean monocyte (Mono) count for the Group I (800/mm^3) is higher than the Group II (700/mm^3). The mean platelet (PLT) count for the Group I (248,000/mm^3) is lower than the Group II (259,000/mm^3). There is no significant difference between the groups according to Mono and PLT counts. ($p>0.05$) (Table 2).

The mean GPS value is 0 in 9 patients, 1 in 25 patients, and 2 in 29 patients for the Group I and 0 in 44 patients, 1 in 10 patients, and 2 in 9 patients for the Group II. Therefore, higher GPS values have significant positive predictive value for the complications of AC (Table 3).

Gallstones were a cause of AC in 48 (76.19%) patients of the Group I and in 58 (92.06%) patients of the Group II. Comorbidities such as diabetes mellitus (DM) and cardiovascular diseases were seen in 49 (77.7%) patients of Group I and 28 (44.4%) patients of Group II. Therefore, we can say that acalculous cholecystitis patients with comorbidities have higher positive predictive value for the complications than the calculous cholecystitis patients without any comorbidities (Table 4).

Table 3. Comparison of GPS values between the two groups

GPS	Group I (Number of patients)	Group II (Number of patients)
0	9 (14.2%)	44 (69.8%)
1	25 (39.6%)	10 (15.8%)
2	29 (46%)	9 (14.2%)

GPS: Glasgow Prognostic Score.

Table 4. Comparison of concomitant gallstone and comorbidities (DM and cardiovascular diseases) between two groups

	Group I (Number of Patients)	Group II (Number of Patients)
Gallstone	48 (76.19%)	58 (92.06%)
Comorbidities (DM± Cardiovascular disease)	49 (77.7%)	28 (44.4%)

DM: Diabetes mellitus.

The thickness of gallbladder wall in patients of Group I (5.25 mm) is higher than the Group II (3.39 mm). Thus, the thickness of the gallbladder has significant positive predictive value for the complications of AC. Perforation of the gallbladder is seen at the time of diagnosis in 17 (%26.9) patients of Group I and no perforation is seen in the Group II.

The cutoff values were determined for the SIRI, SII, PNI, and GPS in each group by the help of ROC analysis. The area under the curve (AUC) value for SIRI is 0.7712 and optimal cutoff value is ≥3955.56. For the cholecystostomy, the sensitivity of the SIRI test is 85.7%, the specificity of the SIRI test is 66.7%, the positive predictive value of the SIRI test is 72.0%, and the negative predictive value of the SIRI test is 82.3% (Fig. 1).

The AUC value for SII is 0.7701 and optimal cutoff value is ≥0.0013. For the cholecystostomy, the sensitivity of the SII test is 87.3%, the specificity of the SII test is 67.5%, the positive predictive value of the SII test is 70.5%, and the negative predictive value of the SII test is 83.3% (Fig. 1).

The AUC value for PNI is 0.8089 and optimal cutoff value is ≤37.51. For the cholecystostomy, the sensitivity of the PNI test is 88.9%, the specificity of the PNI test is 66.7%, the positive predictive value of the PNI test is 72.7%, and the negative predictive value of the PNI test is 85.7% (Fig. 1).

The AUC value for GPS is 0.8487 and optimal cutoff value is ≥1. For the cholecystostomy, the sensitivity of the GPS test is 93.7%, the specificity of the GPS test is 69.8%, the positive predictive value of the GPS test is 75.6%, and the negative predictive value of the GPS test is 91.7% (Fig. 1).

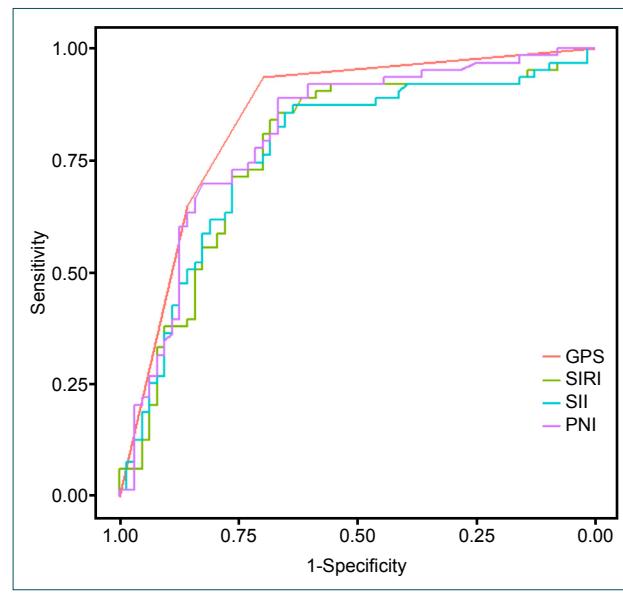

Figure 1. Receiver operating characteristic analysis of the systemic inflammatory response index, systemic inflammation index, prognostic nutritional index, and Glasgow prognostic score for the cholecystostomy.

DISCUSSION

The management of patients with AC who have comorbidities such as DM and cardiovascular diseases represents a difficult clinical challenge for surgeons. Per the 2013 Tokyo Guidelines, patients with Grade III cholecystitis should be managed with optimal medical treatment by means of PC tube drainage. The 2013 Tokyo Guidelines also recommend delayed elective cholecystectomy when cholecystectomy is indicated.[6,14] In our study, the patients with delayed diagnosis of AC (72 h later than onset of the abdominal pain) were managed by medical treatment. If the clinical situation of the patient worsened or was refractory to the medical treatment during the follow-up in hospital, we used PC tube drainage technique to manage the AC and its complications in optimal situations.

In this study, patients who had a delayed diagnosis of AC or had comorbidities did not seem such as viable candidates for an emergency cholecystectomy; therefore, we managed these patients by the help of medical treatment. During the following period in hospital, 63 patients required cholecystostomy and the other 63 patients were managed successfully through medical treatments without invasive procedures like cholecystostomy.

When we compare the age and gender for these two groups, we can see that older patients, and male patients required cholecystostomy tube application significantly more frequently than the younger and female patients ($p<0.001$). Therefore, we can say that older age and male gender may be accepted as positive predictive value for the application of cholecystostomy tube.

Some studies have shown that inflammatory markers such as NLR, PLR, MNR, and immune-based prognostic indexes such as SIRI and SII can be used to evaluate the prognosis of breast cancer.[15,16] They have shown that these inflammatory parameters were associated with poor prognosis of breast cancer, but the mechanism was unclear. Another study by Chen et al.[17] showed that SIRI might serve as an independent prognostic predictor, and it could be used to better predict the prognosis in patients with localized or locally advanced clear cell renal cell carcinoma.

In our study, we evaluated LMR, PLR, NLR, and SIRI to compare two groups. NLR, PLR, and SIRI values in Group I were significantly higher than Group II ($p<0.001$), and the LMR value in Group I was significantly lower than Group II ($p<0.001$). Therefore, we can say that we can use NLR, PLR, and SIRI as a positive predictive value and LMR as a negative predictive value to decide application of cholecystostomy tube for the AC patients who are managed by medical treatment.

In another study by Wang and Zhu,[18] the prognostic value of SII for gastric cancer was evaluated. They showed that SII may serve as a convenient, low-cost, and noninvasive prognostic marker for patients after extremely invasive operations for carcinoma of stomach in gastric cancer. Chen et al.[19] showed that elevated SII was correlated with poor OS and recurrence in patients with CRC. They said that SII was a superior prognostic factor for survival outcome compared to NLR and PLR.

We found that SII value in Group I patients was significantly higher than the Group II ($p<0.001$). According to our study, we can say that SII may be accepted as positive predictive value for the application of acute cholecystostomy tube in AC patients who are managed by medical treatment.

Geng et al.[20] found that PNI was significantly associated with the systemic inflammatory response markers NLR, PLR, and LMR with their study. They showed that a low PNI significantly correlated with a shorter overall survival and that PNI was an independent prognostic predictor for overall survival in patients with advanced pancreatic cancer.

When comparing the PNI values in our study, we found that Group I patients had significantly lower values than the Group II ($p<0.001$). Therefore, we can say that the nutritional status of patients is directly negatively proportional to the severity of AC. We can say that PNI also may be accepted as negative predictive value for the application of cholecystostomy tube in AC patients who are managed by medical treatment.

Wang et al.[21] showed that GPS is a simple and useful indicator of postoperative infectious complications. Their study showed that for patients with a high GPS, the improvement of nutritional status and reduction of inflammatory response before surgery can help reduce post-operative infectious complications.

Our study also evaluated GPS values to compare two groups. GPS values in Group I were significantly higher than the Group II ($p<0.001$). GPS value is calculated by the help of albumin and CRP values. Hence, higher CRP values and lower albumin values means higher GPS. Therefore, we can say that GPS values may be accepted as a positive predictive value for the application of cholecystostomy tube in AC patients who are managed by medical treatments.

Conclusion

According to our study, we can say that NLR, PLR, SII, SIRI, and GPS are positive predictors and LMR and PNI are negative predictors for the severity of AC. When deciding to treat AC medically, we may prefer the application of cholecystostomy tube at the beginning of hospitalization to help evaluate NLR, PLR, LMR, SIRI, SII, GPS, and PNI values.

Ethics Committee Approval: This study was approved by the Trakya University Faculty of Medicine Scientific Research Ethics Committee (Date: 14.06.2021, Decision No: 13/18).

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ORİJİNAL ÇALIŞMA - *ÖZ*

Akut kolesistitli hastalarda SIRI, SII, PNI VE GPS değerlerinin kolesistostomi uygulamasındaki prediktif rolü

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AMAÇ: Akut kolesistitli hastalarda ilk yatış esnasındaki SIRI (Systemic Inflammatory Response Index), SII (Systemic Inflammation Index), PNI (Prognostic Nutritional Index) ve GPS (Glasgow Prognostic Score) değerlerinin, akut kolesistitli hastlarda kolesistostomi uygulaması kararının verilmesindeki klinik değerini araştırmak hedeflenmiştir.

GEREÇ VE YÖNTEM: Ocak 2018 ile Aralık 2020 tarihleri arasında Trakya Üniversitesi Tıp Fakültesi'nde kolesistostomi uygulanmasından bağımsız olarak akut kolesistit tanısı almış olan 126 ardışık hastanın dosyaları retrospektif olarak değerlendirildi. Grup I kolesistostomi uygulanmış hastalardan, Grup II ise kolesistostomi uygulanmamış akut kolesistit tanılı hastalardaı içermektedir. Nötrofil/lenfosit oranı (NLR), trombosit/lenfosit oranı (PLR), lenfosit/monosit oranı (LMR), PNI, GPS ve SII değerleri her iki grup için de hesaplanmıştır.

BULGULAR: İki grup arasında SIRI, SII, PNI ve GPS değerleri arasında anlamlı fark ($p<0.001$) saptandı. Grup I'de SIRI, SII ve GPS değerlerinin Grup II ye göre daha yüksek olduğu görülürken, PNI değerinin is Grup I'de Grup II'ye göre daha düşük olduğu görülmüştür. Ayrıca NLR ve PLR değerleri de Grup I'de Grup II'ye göre belirgin şekilde yüksek saptanırken, LMR değeri ise Grup I'de Grup II'ye belirgin olarak düşük bulunmuştur.

TARTIŞMA: Yaptığımız çalışmaya göre akut kolesistitin klinik şiddeti için NLR, PLR, SII, SIRI ve GPS değerleri pozitif prediktif faktör olarak, LMR ve PNI negatif prediktif faktör olarak değerlendirilmiştir. Dolayısıyla akut kolesistit tanılı bir hasta medikal tedavi için hastaneye yatırıldığında bakılacak olan NLR, PLR, LMR, SII, SIRI, GPS ve PNI değerleri yardımıyla hastanın erken dönemde kolesistostomi ihtiyacı olup olmayacağı saptanabilir.

Anahtar sözcükler: GPS; kolesistit; kolesistostomi; PNI; SII; SIRI.

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