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ORIGINAL RESEARCH

# The Predictive Value of Systemic Inflammatory **Biomarkers in Predicting Postoperative Systemic** Inflammatory Response Syndrome After Percutaneous Nephrolithotomy

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Purpose: The aim of the study was to evaluate the predictive significance of several systemic inflammatory biomarkers, namely neutrophilto-lymphocyte ratio (NLR), lymphocyte-to-monocyte ratio (LMR), platelet-to-lymphocyte ratio (PLR) and systemic immune inflammatory index (SII) in relation to the occurrence of systemic inflammatory response syndrome (SIRS) after percutaneous nephrolithotomy (PCNL). Methods: A cohort of 317 patients who underwent PCNL were retrospectively recruited and evaluated. Based on the subsequent occurrence of SIRS after PCNL, patients were divided into two different groups: SIRS (n = 51) and non-SIRS (n = 266). We examined the effect of neutrophil-to-lymphocyte ratio(NLR), lymphocyte-to-monocyte ratio(LMR), platelet-to-lymphocyte ratio(PLR), and systemic immunoinflammatory index (SII), as well as other demographic characteristics and surgical factors to predict the development of SIRS. Univariate analysis and multivariate logistic regression were used to identify independent predictors of SIRS after PCNL. In addition, receiver operating characteristic (ROC) curves were constructed and area under the curve (AUC) values were calculated to evaluate and compare the discriminatory ability of the studied systemic inflammatory biomarkers.

**Results:** The NLR, PLR, and SII values in the SIRS group were significantly increased compared to those in the non-SIRS group. Multivariate analysis revealed NLR (OR = 1.292, 95% CI: 1.047–1.594, P = 0.017), PLR (OR = 1.008, 95% CI: 1.001–1.016, P = 0.032) and SII (OR = 1.001, 95%CI: 1.000–1.003, P = 0.016) as independent predictors of SIRS development after PCNL. Furthermore, ROC curve analysis highlighted the discriminative ability of NLR, PLR and SII with AUC values of 0.638, 0.644 and 0.680, respectively.

Conclusion: These results highlight the importance of preoperative NLR, PLR and SII as reliable indicators for risk prediction of SIRS after PCNL. In response to these findings, it is critical to perform careful and comprehensive preoperative evaluations of these patients while developing tailored treatment strategies.

Keywords: systemic inflammatory biomarkers, percutaneous nephrolithotomy, systemic inflammatory response syndrome

# Introduction

Urolithiasis is a common disease in urology and represents one of the numerous factors that significantly contribute to a deterioration in quality of life. The prevalence in the entire population is between 5 and 10% over the course of their life.<sup>1</sup> Since this disease has a 50% lifetime chance of recurrence, it is generally recognized as a recurrent disease.<sup>2</sup> Due to its beneficial properties, including exceptional stone-free outcomes and accelerated recovery, percutaneous nephrolithotomy (PCNL) has emerged as the preferred therapeutic modality for the treatment of staghorn stones, complicated stone configurations, and the vast majority of upper urinary tract stones larger than 20 mm in diameter.<sup>3</sup> Despite its advantages, it has a significantly increased incidence of postoperative complications, especially infections, compared to other minimally invasive urinary stone therapies.<sup>4</sup> Complications arising from infection after PCNL include transient fever and manifestation of systemic inflammatory response syndrome (SIRS). Of note, SIRS, as the initial phase of the sepsis cascade, plays a critical role in the eventual progression to full sepsis.<sup>5</sup>

In numerous studies, sepsis has been repeatedly identified as the most serious complication of PCNL. It is the leading cause of postoperative mortality and has a mortality rate between 17.9% and 27.8%.<sup>6,7</sup> Therefore, early detection and timely intervention in SIRS are crucial to reduce the incidence of sepsis and patient mortality after PCNL. Female gender, diabetes mellitus, positive preoperative urine culture, stone size, and the presence of staghorn calculi have been associated with an increased risk of post-PCNL infection. Unfortunately, these factors have repeatedly failed to be identified in all studies and have only limited predictive value.<sup>8,9</sup> Therefore, there is an urgent need for a preoperative predictor that accurately identifies patients at increased risk and allows them to be monitored more intensively. Numerous studies have highlighted the intricate relationships between inflammatory biomarkers and a wide range of diseases and highlighted the promising potential of preoperative inflammatory biomarkers in predicting patient risk.<sup>10–12</sup> Hayıroğlu Mİ, et al found that SII may be an independent predictive marker for both long-term mortality and appropriate intracardiac defibrillator therapy in patients with heart failure with reduced ejection fraction.<sup>13</sup> However, to date there has been a lack of reports specifically addressing systemic inflammatory biomarkers in patients with urinary stones. Our aim in this study was to investigate and identify the preoperative risk factors that predispose patients to the development of SIRS after PCNL and to evaluate the predictive role of NLR, LMR, PLR and SII. By utilizing these systemic inflammatory markers, prevention strategies aimed at reducing the risk of SIRS after PCNL can be developed. In addition, they are routinely measured and inexpensive to test, so they may provide easily accessible, objective information to help physicians assess patient prognosis.

## **Materials and Methods**

#### Clinical Data

This study was approved by the Dongcheng Branch of the First Affiliated Hospital of Anhui Medical University. All methods used in this study strictly adhered to relevant guidelines and regulations. Our hospital's institutional review board granted a waiver from the requirement for written informed consent because this retrospective study used only anonymized patient data and thus poses no risk to individual patients. The data came from our hospital's electronic medical record system. Patients with immunosuppressive diseases, horseshoe kidneys, tumors, malignant hematopathy, end-stage renal disease, and incomplete laboratory data were carefully excluded from the study to ensure the accuracy and integrity of our analysis. To avoid data bias, all operations were performed by two experienced surgeons skilled in PCNL in this study, and the PCNL procedures were conducted through a single tract. A total of 317 patients who underwent PCNL at our center between January 2018 and June 2024 were identified, and their clinical data were subjected to thorough review and analysis. We then divided the patients into two different groups: the SIRS group and the non-SIRS group based on whether they developed SIRS postoperatively. A comprehensive medical history was carefully obtained from each patient, followed by a thorough physical examination, urinalysis, midstream urine culture, complete blood count, and a battery of biochemical blood tests, all performed prior to surgery. Demographic data collected included age, body mass index (BMI), and a comprehensive assessment of comorbidities, particularly hypertension and diabetes mellitus. NLR, LMR, PLR and SII were also calculated at this time. The stone load was calculated using the following formula: length (mm)  $\times$  width (mm)  $\times \pi \times 0.25$ . Stones in the upper urinary tract that affect the renal pelvis and extend into at least two calyces are classified as staghorn stones. The main focus of the study was to assess whether patients developed SIRS after PCNL. SIRS was defined as the development of two or more of the following conditions: (1) core temperature  $>38^{\circ}$ C or  $<36^{\circ}$ C, (2) heart rate >90 beats/minute, (3) respiratory rate >20 breaths/minimum or partial pressure of carbon dioxide (PaCO2) <32 mmHg, (4) white blood cell count >12,000 cells/ml or <4000 cells/ml.<sup>14</sup> Preoperative examinations routinely included renal-ureter-bladder radiography (KUB), ultrasonography, and either computed tomography (CT) or intravenous urography (IVU) to assess patient status. Patients with preoperative urinary tract infections or positive preoperative urine cultures were administered appropriate antibiotics for full treatment courses (3-7 days) based on the results of culture and antibiogram tests. Patients with sterile urine received broad-spectrum prophylactic antibiotics 30 minutes before surgery. Subsequently, the perioperative clinical data of these patients were carefully recorded and analyzed retrospectively.

#### Surgical Procedure

After the anesthesia took effect, the patient was positioned in the lithotomy position, and then a 5 Fr ureteral catheter was inserted. Following this, the patient was repositioned in the prone position. Guided by ultrasonography, an appropriate renal calyx was punctured to establish the optimal percutaneous access path. Subsequently, an 18 Fr sheath was placed. The stones were fragmented with a Holmium laser using an 8/9.8F semi-rigid ureteroscope. The extraction process involved careful removal of the larger stone fragments using stone forceps, while the smaller fragments were efficiently removed using a pulsed perfusion pump. At the conclusion of each procedure, a double-J catheter and nephrostomy tube were carefully positioned.

## Statistical Analysis

Statistical analysis was performed using version 23.0 of SPSS software (IBM Corp, Armonk, NY, USA). The Kolmogorov-Smirnov (K-S) test was used to determine whether the data variables had a normal or non-normal distribution pattern. Categorical variables were analyzed using either the chi-square test or Fisher's exact test, depending on the characteristics of the data. Independent samples *t*-test was used to analyze normally distributed numerical variables, while Mann-Whitney U test was used for skewed data. Categorical data is presented as numbers and percentages. A combination of univariate and multivariate logistic regression analyzes was used to identify the independent factors significantly associated with the development of SIRS after PCNL. The Hosmer-Lemeshow test indicated good calibration when the test was not significant. Receiver operating characteristic (ROC) curves were then recorded and area under the curve (AUC) values were calculated to evaluate and compare the discriminative power of the systemic inflammation biomarkers. The Youden index (J = [sensitivity + specificity] - 1) was used to determine the optimal predictive cutoffs for calculating AUC values. A two-sided *p* value <0.05 was considered statistically significant.

# Results

A total of 317 patients (201 men, 116 women) who had previously undergone PCNL were included in the study. The median (IQR) age of patients was 55.0 (47.0–66.0) years. A total of 51 patients (16.1% of the total) developed SIRS postoperatively. When conducting the Mann-Whitney U test or Chi-square test on the selected 27 factors, we found that 10 of these factors have a significant correlation with SIRS. Notably, the differences in NLR, PLR, LMR, and SII values between the two groups reached statistical significance with a P value of less than 0.05. In addition, the two groups also differed significantly in female sex, blood leukocytes, blood neutrophils, positive urine leukocytes, urine nitrite and urine culture (P < 0.05). All data are listed in Table 1.

Univariate analysis revealed a significant correlation between the development of post-PCNL SIRS and a specific set of variables, including female gender, operation time, blood leukocyte count, blood neutrophil level, blood monocyte concentration, urine leukocyte count, urine nitrite, urine culture results, as well as NLR, PLR, LMR and SII indices on the variables examined. Furthermore, multivariate analysis showed that NLR (OR=1.292, 95% CI: 1.047–1.594, P = 0.017), PLR (OR=1.008, 95% CI:

Variables	SIRS (n=51)	Non-SIRS (n=266)	P value
Age, median (IQR); (years)	55.00(48.00–66.00)	54.50(46.00-66.00)	0.447
Sex (male/female); n (%)			
Male	21(41.2%)	180(67.7%)	<0.001
Female	30(58.8%)	86(32.3%)	
BMI, median (IQR); (kg/m²)	24.03(21.23-27.47)	24.34(21.97-26.54)	0.561
Blood total Cholesterol, median (IQR); (mmol/L)	4.620(3.980-5.020)	4.575(4.078-5.353)	0.326
Hypertension; n (%)			
Yes	16(31.4%)	70(26.3%)	0.457
No	35(68.6%)	196(73.7%)	

Table	I	Demographic	and	Clinical	Data	of All	Patients
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(Continued)

Table I	(Continued).
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Variables	SIRS (n=51)	Non-SIRS (n=266)	P value
Diabetes; n (%)			
Yes	7(13.7%)	26(9.8%)	0.397
No	44(86.3%)	240(90.2%)	
Staghorn calculi; n (%)			
Yes	10(19.6%)	31(11.7%)	0.121
No	41(80.4%)	235(88.3%)	
Stone burden, median (IQR); (mm²)	259.17 (157.08-373.05)	220.30(157.08-314.15)	0.368
Stone laterality			
Left (%)	25(49.0%)	149(56.0%)	0.358
Right (%)	26(51.0%)	117(44.0%)	
Hydronephrosis, n (%)			
Yes	46(90.2%)	228(85.7%)	0.392
No	5(9.8%)	38(14.3%)	
Operative time, median (IQR); (min)	98.00(75.00-120.00)	90.00(70.00-107.50)	0.183
Urine leukocyte			
Positive	43(84.3%)	164(61.7%)	0.002
Negative	8(15.7%)	102(38.3%)	
Urine nitrite			
Positive	12(23.5%)	I 3(4.9%)	<0.001
Negative	39(76.5%)	253(95.1%)	
Urine culture; n (%)			
Positive	15(29.4%)	17(6.4%)	<0.001
Negative	36(70.6%)	249(93.6%)	
Blood urea nitrogen, median (IQR); (mmol/L)	5.670(4.580-7.630)	5.685(4.665-6.795)	0.814
Blood creatinine, median (IQR); (umol/L)	68.700(58.200-103.500)	75.800(63.750-92.350)	0.536
Blood eGFR, median (IQR); (mL/min)	99.000(68.000-112.000)	99.000(79.750-111.000)	0.790
Blood leukocyte, median (IQR); (10 <sup>9</sup> /L)	6.620(5.620-8.350)	5.940(5.075-7.295)	0.011
Blood neutrophil, median (IQR); (10 <sup>9</sup> /L)	4.200(3.200-5.600)	3.450(2.700-4.500)	0.002
Blood lymphocyte, median (IQR); (10 <sup>9</sup> /L)	1.660(1.160-1.990)	1.745(1.320-2.130)	0.114
Blood monocyte, median (IQR); (10 <sup>9</sup> /L)	0.490(0.410-0.690)	0.480(0.400-0.600)	0.220
Blood platelet, median (IQR); (10 <sup>9</sup> /L)	189.00(161.00-234.00)	184.00(148.50-219.00)	0.122
Blood hemoglobin, median (IQR); (g/L)	131.00(119.00-143.00)	134.00(126.00–144.25)	0.139
NLR, median (IQR)	2.63(1.92-3.93)	1.94(1.48–2.81)	0.002
PLR, median (IQR)	123.88(102.50-163.80)	104.12(83.48–132.07)	0.001
LMR, median (IQR)	2.81 (2.22-4.14)	3.68(2.69-4.74)	0.015
SII, median (IQR)	516.49(344.91-743.19)	376.54(259.85-523.69)	<0.001

1.001–1.016, P = 0.032), SII (OR=1.001, 95% CI: 1.000–1.003, P = 0.016), female gender (OR = 0.337, 95% CI: 0.168–0.677, P = 0.002), operation time (OR = 1.015, 95% CI: 1.002–1.028, P = 0.021) and urine culture (OR = 3.992, 95% CI: 1.349–11.818, P = 0.012) were all independent predictors of SIRS after PCNL. All data are listed in Table 2.

The calibration curve shows that the model fits well, which is supported by the nonsignificant result (P = 0.251) of the Hosmer-Lemeshow test. The ROC curve was constructed using SPSS software and was based on both the predicted probability and actual cases of postoperative SIRS occurrence. AUC values were then used to evaluate and compare the predictive abilities of the biomarkers for systemic inflammation. The cutoff value for preoperative NLR for predicting postoperative SIRS was 2.09, with a sensitivity of 72.5% and specificity of 55.6%, resulting in an AUC of 0.638 (P = 0.002). The cutoff value for PLR for predicting postoperative SIRS was 107.72, with a sensitivity of 68.6% and specificity of 56.8%, resulting in an AUC of 0.644 (P = 0.001). The cutoff value for SII to predict postoperative SIRS was 594.09, with a sensitivity of 47.1% and specificity of 82.3%, resulting in an AUC of 0.680 (P < 0.001). All of these data are listed in Table 3. The ROC curve plots for NLR, PLR and SII are shown in Figure 1.

Variables	Univariate Analysis		Multivariate Analysis			
	OR	95% CI	P value	OR	95% CI	P value
Age	1.011	0.989–1.034	0.325			
Sex (male/female)	0.334	0.181-0.618	<0.001	0.337	0.168–0.677	0.002*
BMI	0.982	0.905-1.066	0.670			
Total Cholesterol	0.789	0.561-1.110	0.173			
Hypertension	1.280	0.667–2.455	0.458			
Diabetes	1.469	0.600-3.592	0.400			
Staghorn calculi	1.849	0.842-4.058	0.125			
Stone burden	1.001	0.999-1.002	0.119			
Stone laterality	1.324	0.727-2.413	0.359			
Hydronephrosis	1.533	0.573-4.105	0.395			
Operative time	1.013	1.001-1.024	0.027	1.015	1.002-1.028	0.021*
Urine leukocyte	3.343	1.511–7.396	0.003	2.081	0.868–4.987	0.100
Urine nitrite	5.988	2.549-14.066	<0.001	1.555	0.472-5.119	0.468
Urine culture	6.103	2.805-13.278	<0.001	3.992	1.349–11.818	0.012*
Blood urea nitrogen	1.062	0.942-1.198	0.327			
Blood creatinine	1.004	0.996-1.012	0.384			
Blood eGFR	0.997	0.986-1.008	0.606			
Blood leukocyte	1.260	1.053-1.507	0.012	0.797	0.471-1.348	0.397
Blood neutrophil	1.383	1.131–1.692	0.002	1.669	0.956-2.912	0.071
Blood lymphocyte	0.605	0.346-1.056	0.077			
Blood monocyte	5.360	1.180–24.344	0.030	5.902	0.666–52.309	0.111
Blood platelet	1.005	0.999–1.010	0.087			
Blood hemoglobin	0.984	0.967-1.002	0.075			
NLR	1.371	1.138–1.652	0.001	1.292	1.047–1.594	0.017*
PLR	1.009	1.003-1.016	0.006	1.008	1.001-1.016	0.032*
LMR	0.761	0.610-0.949	0.015	0.818	0.617-1.086	0.165
SII	1.002	1.001-1.003	<0.001	1.001	1.000-1.003	0.016*

Table 2 Univariate and Multivariate Analyses for Predicting SIRS After PCNL

Note: \*Values are statistically significant.

 Table 3 Comparison of AUC and Cut-off Values Between the Systemic Inflammation Biomarkers

	AUC	95%CI	P value	Cut-off Value	Sensitivity	Specificity
NLR	0.638	0.549–0.728	0.002	2.09	72.5%	55.6%
PLR	0.644	0.566-0.723	0.001	107.72	68.6%	56.8%
SII	0.680	0.600–0.759	<0.001	594.09	47.1%	82.3%

#### Discussion

Advances in instrumentation and techniques have significantly improved the efficacy and safety profile of PCNL, yet postoperative systemic inflammatory response syndrome (SIRS) remains a common complication in patients undergoing this procedure.<sup>15,16</sup> Previous studies have reported an incidence rate of systemic inflammatory response syndrome (SIRS) ranging from approximately 7.7% to 31.1% after percutaneous nephrolithotomy procedures.<sup>17,18</sup> The incidence of SIRS after PCNL in our study is 16.1% (51/317), which is comparable to previous reports. Therefore, there is an imperative need to carefully evaluate the risk factors that correlate with postoperative infectious complications due to PCNL procedures, prevention and early detection of SIRS are crucial.<sup>19,20</sup> Signs of SIRS may be the result of the body's inflammatory response to the surgical procedure. Several studies have highlighted the crucial role of inflammation in both

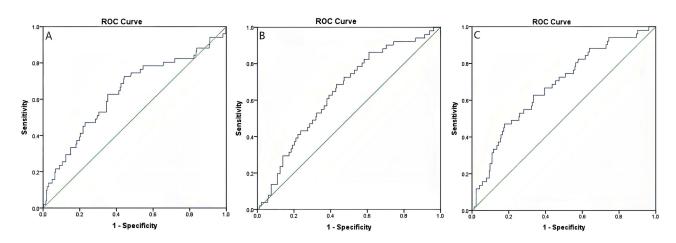


Figure I ROC curves for neutrophil-to-lymphocyte ratio (NLR) (A), platelet-to-lymphocyte ratio (PLR) (B) and Systemic immune-inflammatory index (SII) (C) to predict SIRS. ROC = receiver operating characteristic.

the formation and progression of kidney stones and highlighted the need for further exploration of potential biomarkers and diagnostic approaches that can more accurately assess this inflammatory aspect.<sup>21,22</sup>

In this study, we found that patients with SIRS have higher NLR, PLR, and SII levels than non-SIRS patients. Additionally, in multivariate analysis, preoperative NLR, PLR, and SII each showed a significant association with SIRS occurring after PCNL. In recent studies, The NLR is a marker of systemic inflammation that has been shown to predict adverse cardiovascular events in various diseases. Higher NLR levels have been found to be associated with stent restenosis in patients with bare-metal stents who have stable/unstable angina pectoris and ST-segment elevation myocardial infarction(STEMI).<sup>23</sup> A higher PLR was an independent risk factor for the development of contrastinduced nephropathy(CIN) in patients with STEMI undergoing percutaneous coronary intervention. Considering its clinical significance, the PLR may help identify high-risk candidates of CIN in these patients.<sup>24</sup> Regarding the predictive value of specific biomarkers in stone disease, the presence of stones triggers the release of various inflammatory mediators, including IL-6, IL-7, IL-8, TNF- $\alpha$  and GCSF, which subsequently leads to an increase in neutrophil numbers. The accumulation of cytokines in the tissue microenvironment promotes an environment favorable to the further development of stone formation.<sup>25</sup> Bacterial infection can cause patients to release chemokines, leading to the accumulation of inflammatory cytokines in the tissue microenvironment. This process in turn triggers chemotaxis and vigorously promotes the formation and subsequent release of a significant amount of neutrophils from the bone marrow, ultimately leading to increased neutrophil levels both locally and systemically.<sup>26</sup> Neutrophils are known to be a component of the inflammatory response and can suppress the immune response by inhibiting the cytolytic activity of various immune cells, including lymphocytes, activated natural killer cells and T cells.<sup>25</sup> Platelets are rich in pro-inflammatory agents, which allow them to secrete powerful pro-inflammatory metabolites. Monocytes also play a central role as regulators within the complex systemic inflammatory response.<sup>27,28</sup> Hawkins et al have also revealed that both T and B lymphocytes experience a significant decline in the presence of gram-positive and gram-negative bacteremia.<sup>29</sup> Hu et al were the first to introduce the systemic immune inflammatory index (SII), a groundbreaking inflammatory metric defined as the platelet count multiplied by the neutrophil to lymphocyte ratio and also includes the absolute blood count.<sup>30</sup> The research found that the systemic immune inflammatory index (SII) serves as a strong predictor of adverse outcomes in patients diagnosed with hepatocellular carcinoma. Furthermore, SII has emerged as a promising prognostic tool in the context of colorectal cancer, and there is ample evidence supporting its utility.<sup>31</sup> NLR and PLR consist of combinations of two different inflammatory cell types. In comparison, SII is a biomarker of inflammatory complexes that combines three different inflammatory cell types and is less influenced by physiological conditions. Given the complicated pathogenesis of infectious diseases and diverse clinical manifestations, a multifaceted approach using a combination of multiple biomarkers appears to be the most pragmatic and effective strategy for diagnosis.<sup>32</sup> NLR, PLR, and SII have proven to be valuable tools for identifying systemic inflammation. These markers have been widely used to predict prognosis for

a range of diseases, including malignancies, inflammatory diseases, and cardiovascular diseases.<sup>10,33</sup> The current study used a combinatorial index that allows a comprehensive assessment of all observations across different cell types. Consequently, an increase in NLR, PLR or SII serves as a potential indicator of an active inflammatory response. These markers, derived from a complete blood count, are now part of routine examinations and are inexpensive. The role of these biomarkers in stone crystallization has contributed to the establishment of the theory of stone formation, which includes immune response, oxidative stress and inflammatory cell response.<sup>34</sup>

In multivariate analysis, female gender, preoperative urine cultures, and operation duration were important risk factors for the development of post-PCNL SIRS. A likely reason for this was women's increased susceptibility to infection is their shorter urethra, which is in close proximity to the vagina and anus. This anatomical feature likely contributes to a higher risk of infection. In addition, as women approach menopause, estrogen levels decline, leading to atrophy of the urinary tract mucosa. This reduction in glycogen levels in the epithelial cells can, in turn, potentially increase the risk of infection, subsequently leading to a corresponding decrease in glycogen-dependent vaginal flora and a corresponding increase in Escherichia coli, ultimately leading to urinary tract infections.<sup>35</sup> A positive urine culture conclusively indicates the presence of a preoperative urinary tract infection and highlights the need for prompt attention and treatment. PCNL can cause excessive renal pelvic pressure, leading to pyelotubular, pyelolymphatic, and pyelovenous backflow, which can subsequently lead to bacteria entering the circulation. The risk of SIRS increases with increasing operative time.<sup>35,36</sup> Despite negative urine cultures, some patients still develop SIRS. The occurrence of postoperative sepsis in the absence of bacteremia or bacteriuria could potentially be due to the persistent presence of bacterial endotoxins in infected stones.<sup>21,37</sup> Higher SII, NLR or PLR can be used as indicators to predict SIRS, especially in negative urine cultures. Prompt and aggressive anti-infective treatment during the perioperative period is of paramount importance to prevent the occurrence of SIRS and mitigate its progression toward urosepsis.

#### Conclusions

The complicated pathogenesis of postoperative infections involves several factors that make it a complex phenomenon. Among the countless potential indicators, NLR, PLR and SII emerge as valuable, stand-alone, readily available and economically feasible predictors of the occurrence of SIRS after PCNL. The results of our study may serve as a valuable tool for the preoperative identification of patients at increased risk. The combined use of systemic inflammatory biomarkers provides clinicians with a robust tool for early detection and intervention. Therefore, high-risk patients with an elevated preoperative NLR, PLR, and SII ratio should receive greater attention and consider prolonged antibiotic prophylaxis before surgery, especially those with a negative preoperative urine culture. The use of active anti-infective therapies during the perioperative period, minimization of intraoperative systemic inflammation and infection. To further solidify their clinical significance, further prospective studies are needed to examine the predictive accuracy of these biomarkers compared to other established risk factors.

#### **Abbreviations**

SIRS, Systemic inflammatory response syndrome; PCNL, Percutaneous nephrolithotomy; NLR, Neutrophil to lymphocyte ratio; LMR, lymphocyte to monocyte ratio; PLR, Platelet to lymphocyte ratio; SII, Systemic immune inflammation, platelet count  $\times$  neutrophil count / lymphocyte count; IQR, Interquartile Range.

## **Data Sharing Statement**

The records and data of this study are saved in the patients' secure medical records at the Dongcheng branch of The First Affiliated Hospital of Anhui Medical University. Further inquiries can be directed to Qi Wei.

## **Ethics Approval and Informed Consent**

This study was a retrospective study, and all patient information collection and processing were strictly confidential. Our procedures were carried out in accordance with the Declaration of Helsinki. The ethics committee of the Dongcheng branch of The First Affiliated Hospital of Anhui Medical University approved the study.

# Funding

This study was funded by the National Natural Science Foundation of China (No. 82070724) and the Natural Science Foundation of Anhui Province (No. 1908085MH246).

# Disclosure

The authors declared that they have no conflict of interest.

## References

- 1. Lang J, Narendrula A, El-Zawahry A, Sindhwani P, Ekwenna O. Global trends in incidence and burden of urolithiasis from 1990 to 2019: an analysis of global burden of disease study data. *Eur Urol Open Sci.* 2022;35:37–46. doi:10.1016/j.euros.2021.10.008
- 2. Ferakis N, Stavropoulos M. Mini percutaneous nephrolithotomy in the treatment of renal and upper ureteral stones: lessons learned from a review of the literature. *Urol Ann.* 2015;7(2):141–148. doi:10.4103/0974-7796.152927
- 3. Türk C, Petřík A, Sarica K, et al.. EAU guidelines on diagnosis and conservative management of urolithiasis. Eur Urol. 2016;69(3):468–474. doi:10.1016/j.eururo.2015.07.040
- 4. Seitz C, Desai M, Häcker A, et al.. Incidence, prevention, and management of complications following percutaneous nephrolitholapaxy. *Eur Urol.* 2012;61(1):146–158. doi:10.1016/j.eururo.2011.09.016
- Cetinkaya M, Buldu I, Kurt O, Inan R. Platelet-to-lymphocyte ratio: a new factor for predicting systemic inflammatory response syndrome after percutaneous nephrolithotomy. Urol J. 2017;14(5):4089–4093.
- 6. Martin GS, Mannino DM, Eaton S, Moss M. The epidemiology of sepsis in the United States from 1979 through 2000. N Engl J Med. 2003;348 (16):1546–1554. doi:10.1056/NEJMoa022139
- 7. De la Rosette J, Assimos D, Desai M, et al.; CROES PCNL Study Group. The clinical research office of the endourological society percutaneous nephrolithotomy global study: indications, complications, and outcomes in 5803 patients. *J Endourol.* 2011;25(1):11–17. doi:10.1089/ end.2010.0424
- Chen L, Xu QQ, Li JX, Xiong LL, Wang XF, Huang XB. Systemic inflammatory response syndrome after percutaneous nephrolithotomy: an assessment of risk factors. Int J Urol. 2008;15(12):1025–1028. doi:10.1111/j.1442-2042.2008.02170.x
- 9. Bansal SS, Pawar PW, Sawant AS, Tamhankar AS, Patil SR, Kasat GV. Predictive factors for fever and sepsis following percutaneous nephrolithotomy: a review of 580 patients. Urol Ann. 2017;9(3):230-233. doi:10.4103/UA.UA 166 16
- Bahadır A, Baltacı D, Türker Y, et al.. Is the neutrophil-to-lymphocyte ratio indicative of inflammatory state in patients with obesity and metabolic syndrome?. Anatol J Cardiol. 2015;15(10):816–822. doi:10.5152/akd.2014.5787
- 11. Kahraman C, Kahraman NK, Aras B, Coşgun S, Gülcan E. The relationship between neutrophil-to-lymphocyte ratio and albuminuria in type 2 diabetic patients: a pilot study. Arch Med Sci. 2016;12(3):571–575. doi:10.5114/aoms.2016.59931
- 12. Yasar Z, Buyuksirin M, Ucsular FD, et al. Is an elevated neutrophil-to-lymphocyte ratio a predictor of metabolic syndrome in patients with chronic obstructive pulmonary disease?. Eur Rev Med Pharmacol Sci. 2015;19(6):956–962.
- 13. Hayıroğlu Mİ, Çınar T, Çinier G, et al. Evaluating systemic immune-inflammation index in patients with implantable cardioverter defibrillator for heart failure with reduced ejection fraction. *Pacing Clin Electrophysiol.* 2022;45(2):188–195. doi:10.1111/pace.14436
- 14. Jang DI, Lee AH, Shin HY, et al.. The role of tumor necrosis factor Alpha (TNF-α) in autoimmune disease and current TNF-α inhibitors in therapeutics. *Int J Mol Sci.* 2021;22(5):2719. doi:10.3390/ijms22052719
- Omar M, Noble M, Sivalingam S, et al.. Systemic inflammatory response syndrome after percutaneous nephrolithotomy: a randomized single-blind clinical trial evaluating the impact of irrigation pressure. J Urol. 2016;196(1):109–114. doi:10.1016/j.juro.2016.01.104
- Lotan P, Goldberg H, Nevo A, et al.. Post-operative pain following percutaneous nephrolithotripsy- clinical correlates. Urologia. 2023;90 (3):503–509. doi:10.1177/03915603221130899
- 17. Chen D, Jiang C, Liang X, et al.. Early and rapid prediction of postoperative infections following percutaneous nephrolithotomy in patients with complex kidney stones. *BJU Int.* 2019;123(6):1041–1047. doi:10.1111/bju.14484
- 18. Koras O, Bozkurt IH, Yonguc T, et al.. Risk factors for postoperative infectious complications following percutaneous nephrolithotomy: a prospective clinical study. *Urolithiasis*. 2015;43(1):55-60. doi:10.1007/s00240-014-0730-8
- 19. Wang M, Yang Z, He N, Wang D, Lan H. Predictive model of systemic inflammatory response syndrome after percutaneous nephrolithotomy for kidney calculi based on logistic regression. *Am J Transl Res.* 2023;15(6):4138–4146.
- 20. Tokas T, Herrmann TRW, Skolarikos A, Nagele U. Training and research in urological surgery and technology (T.R.U.S.T.)-Group. Pressure matters: intrarenal pressures during normal and pathological conditions, and impact of increased values to renal physiology. World J Urol. 2019;37 (1):125–131. doi:10.1007/s00345-018-2378-4
- 21. McAleer IM, Kaplan GW, Bradley JS, Carroll SF, Griffith DP. Endotoxin content in renal calculi. J Urol. 2003;169(5):1813–1814. doi:10.1097/01. ju.0000061965.51478.79
- 22. Mulay SR, Kulkarni OP, Rupanagudi KV, et al.. Calcium oxalate crystals induce renal inflammation by NLRP3-mediated IL-1β secretion. J Clin Invest. 2013;123(1):236–246. doi:10.1172/JCI63679
- 23. Avci II, Sahin I, Gungor B, et al. Association of monocyte to high-density lipoprotein ratio with bare-metal stent restenosis in STEMI patients treated with primary PCI. North Clin Istanb. 2018;6(4):393-400. doi:10.14744/nci.2018.93653
- 24. Sun XP, Li J, Zhu WW, et al.. Platelet to lymphocyte ratio predicts contrast-induced nephropathy in patients with ST-segment elevation myocardial infarction undergoing primary percutaneous coronary intervention. *Angiology*. 2018;69(1):71–78. doi:10.1177/0003319717707410
- 25. Tang K, Liu H, Jiang K, et al.. Predictive value of preoperative inflammatory response biomarkers for metabolic syndrome and post-PCNL systemic inflammatory response syndrome in patients with nephrolithiasis. *Oncotarget*. 2017;8(49):85612–85627. doi:10.18632/oncotarget.20344
- 26. Chousterman BG, Swirski FK, Weber GF. Cytokine storm and sepsis disease pathogenesis. Semin Immunopathol. 2017;39(5):517-528. doi:10.1007/s00281-017-0639-8

- Gasparyan AY, Ayvazyan L, Mukanova U, Yessirkepov M, Kitas GD. The platelet-to-lymphocyte ratio as an inflammatory marker in rheumatic diseases. Ann Lab Med. 2019;39(4):345–357. doi:10.3343/alm.2019.39.4.345
- Lee JS, Kim NY, Na SH, Youn YH, Shin CS. Reference values of neutrophil-lymphocyte ratio, lymphocyte-monocyte ratio, platelet-lymphocyte ratio, and mean platelet volume in healthy adults in South Korea. *Medicine*. 2018;97(26):e11138. doi:10.1097/MD.000000000011138
- Hawkins CA, Collignon P, Adams DN, Bowden FJ, Cook MC. Profound lymphopenia and bacteraemia. Intern Med J. 2006;36(6):385–388. doi:10.1111/j.1445-5994.2006.01076.x
- Hu B, Yang XR, Xu Y, et al.. Systemic immune-inflammation index predicts prognosis of patients after curative resection for hepatocellular carcinoma. *Clin Cancer Res.* 2014;20(23):6212–6222. doi:10.1158/1078-0432.CCR-14-0442
- Passardi A, Azzali I, Bittoni A, et al.. Inflammatory indices as prognostic markers in metastatic colorectal cancer patients treated with chemotherapy plus Bevacizumab. *Ther Adv Med Oncol.* 2023;15:17588359231212184. doi:10.1177/17588359231212184
- 32. Cohen J, Vincent JL, Adhikari NK, et al.. Sepsis: a roadmap for future research. Lancet Infect Dis. 2015;15(5):581-614. doi:10.1016/S1473-3099(15)70112-X
- Ozyalvacli ME, Ozyalvacli G, Kocaaslan R, et al.. Neutrophil-lymphocyte ratio as a predictor of recurrence and progression in patients with high-grade pT1 bladder cancer. Can Urol Assoc J. 2015;9(3–4):E126–31. doi:10.5489/cuaj.2523
- 34. Mao W, Wu J, Zhang Z, Xu Z, Xu B, Chen M. Neutrophil-lymphocyte ratio acts as a novel diagnostic biomarker for kidney stone prevalence and number of stones passed. *Transl Androl Urol.* 2021;10(1):77–86. doi:10.21037/tau-20-890
- 35. Zhou G, Zhou Y, Chen R, et al. The influencing factors of infectious complications after percutaneous nephrolithotomy: a systematic review and meta-analysis. Urolithiasis. 2022;51(1):17. doi:10.1007/s00240-022-01376-5
- 36. Kreydin EI, Eisner BH. Risk factors for sepsis after percutaneous renal stone surgery. Nat Rev Urol. 2013;10(10):598-605. doi:10.1038/ nrurol.2013.183
- 37. Desai M, De Lisa A, Turna B, et al.; Rosette On Behalf Of The Croes Pcnl Study Group J. The clinical research office of the endourological society percutaneous nephrolithotomy global study: staghorn versus nonstaghorn stones. J Endourol. 2011;25(8):1263–1268. doi:10.1089/end.2011.0055

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