Platelet-to-Lymphocyte Ratio: A New Factor for Predicting Systemic Inflammatory Response Syndrome after Percutaneous Nephrolithotomy

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Purpose: The first purpose of this study was to reveal factors affecting the postoperative development of systemic inflammatory response syndrome (SIRS) in patients undergoing standard percutaneous nephrolithotomy (PNL) for renal stones. The second purpose was to determine the role of the preoperative platelet-to-lymphocyte ratio (PLR) and the neutrophil-to-lymphocyte ratio (NLR) in the prediction of SIRS.

Matarials and Methods: In total, 192 patients who had undergone conventional PNL for renal stones from 2013 to 2015 were included in the study. SIRS developed postoperatively in 41 (21.3%) patients. The patients were divided into SIRS and non-SIRS groups, and the effects of the PLR, NLR, and other demographic and operative data were investigated to predict the development of SIRS. Variables significant in the univariate analysis were evaluated using a multiple logistic regression model to determine the independent risk factors for developing SIRS after PNL.

Results: Univariate analysis revealed significant differences in the preoperative PLR ($P < .001$), preoperative NLR ($P = .018$), number of access sites ($P < .001$), mean renal parenchymal thickness ($P = .02$), operative time ($P < .001$), decrease in hemoglobin ($P = .016$), length of hospital stay ($P < .001$), stone-free status ($P = .023$), and complication rate between the two groups of patients. However, multivariate analysis showed that only the PLR and the number of access sites were independent factors affecting the development of SIRS. When the PLR cut-off value was 114.1, development of SIRS was predicted with 80.4% sensitivity and 60.2% specificity.

Conclusion: The preoperative PLR is an effective and inexpensive biomarker with which to predict SIRS after PNL. In particular, we recommend close monitoring of patients with a PLR of >114.1 because of the possible development of serious complications.

Keywords: inflammation; kidney; lymphocyte; nephrolithotomy; nephrolithiasis; platelet ratio; systemic inflammatory response syndrome

INTRODUCTION

Percutaneous nephrolithotomy (PNL) is a minimally invasive technique recommended as first-line treatment for renal stones > 2 cm in diameter because it has a high success rate.[1] However, PNL is associated with some complications. Among them, sepsis occurs in 0.3% to 3.1% of patients[2], and reported mortality rates range from 25% to 50%.[3,4] Sepsis prolongs the hospitalization period and increases treatment costs. Systemic inflammatory response syndrome (SIRS) is closely associated with the development of sepsis and results in both infectious and noninfectious inflammation. The platelet-to-lymphocyte ratio (PLR) and the neutrophil-to-lymphocyte ratio (NLR) are biomarkers that increase during inflammation. Various studies have evaluated the role of the PLR and NLR in many oncological diseases.[5-8] Some studies have investigated factors affecting SIRS and the febrile state after PNL.[9,10] In this study, we investigated for the first time whether the preoperative PLR and NLR are effective inflammatory markers with which to predict the occurrence of SIRS after PNL.

MATERIALS AND METHODS

Study Population

In total, 192 patients (61 female and 131 male) who had undergone conventional PNL in a single center to treat renal stones from 2013 to 2015 were included in the study. The patients' medical records were evaluated retrospectively. The patients were divided into a non-SIRS group (Group 1) and SIRS group (Group 2) based on whether they developed SIRS postoperatively. Children aged < 18 years, patients with at least one SIRS criterion during the preoperative evaluation, patients with an oncological disease or previously placed nephrostomy tube or urinary stent, patients who had undergone ipsilateral or contralateral ureteroscopic intervention and bilateral standard PNL in the same session, and patients

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Table 1. Demographic and operative data of the patients enrolled into the study.

	Overall	Group 1	Group 2	*P*-Value
Patient number (N)	192	151	41	
Age (years); mean ± SD	47.3±15.1	47.4±30.1	47.2±32.9	.967
Sex (Male/Female); N (%)				.424
-Male	131 (68.2%)	104 (68.9%)	27 (65.9%)	
-Female	61 (31.8%)	47 (31.1%)	14 (34.1%)	
Previous stone treatment; N (%)	56 (29.1%)	46 (30.4%)	10 (24.4%)	.255
-SWL	33 (17.2%)	26 (17.2%)	7 (17.1%)	
-PNL	19 (9.9%)	17 (11.2%)	2 (4.8%)	
-Open surgery	4 (2.0%)	3 (2.0%)	1 (2.4%)	
Diabetes Mellitus; N (%)	25 (13%)	22 (14.6%)	3 (7.3%)	.169
Preop PLR; mean ± SD	116.7 ± 39.9	109.3 ± 34.3	142.9 ± 47.3	< 0.001
Preop NLR; mean ± SD	2.6±1.5	2.4±1.4	3.1±1.9	.018
Hydronephrosis; N (%)				.065
-Absent	42 (21.9)	37 (24.5%)	5 (12.2%)	
-Present	150 (78.1)	114 (75.5%)	36 (87.8%)	
Stone Location; N (%)				.246
-Pelvis	40 (20.8%)	31 (20.5%)	9 (22%)	
-Calix	39 (20.3%)	34 (22.5%)	5 (12.2%)	
-Pelvis + Calix	63 (32.8%)	51 (33.8%)	12 (29.3%)	
-Staghorn	50 (26%)	35 (23.2%)	15 (36.6%)	
Parenchymal Thickness (mm); mean ± SD	17.4 ± 4.4	17.8 ± 4.5	15.9 ± 4.1	.020
BMI (kg/m²); mean ± SD	28.5 ± 5.1	28.8 ± 5.2	27.4 ± 4.3	.124
ASA score; mean ± SD	1.39 ± 0.55	1.40 ± 0.54	1.37 ± 0.58	.695
Stone size (mm²); mean ± SD	675.9 ± 619.1	652.7 ± 632.6	765.7 ± 567.0	.311
Access Number; N (%)				< 0.001
-Single	175 (91.1%)	145 (96%)	30 (73.2%)	
-Multiple	17 (8.9%)	6 (4%)	11 (26.8%)	
Operative time (minutes); mean ± SD	52.0 ± 31.8	47.4 ± 30.1	68.6 ± 32.9	< 0.001
Hemoglobin drop (mg/dL); mean ± SD	2.3 ± 1.3	2.2 ± 1.1	2.7 ± 1.7	.016
Tubeles; N (%)	.304			
-Yes	26 (13.5%)	22 (14.6%)	4 (9.8%)	
-No	166 (86.5%)	129 (85.4%)	37 (91.2%)	
Complication; N (%)				.019
-Minor	19 (79.2%)	12 (100%)	7 (58.3%)	
-Major	5 (20.8%)	0	5 (41.7%)	
Hospital stay (day); mean ± SD	1.88 ± 1.0	1.58 ± 0.8	3.0 ± 1.1	< 0.001
Stone Free; N (%)				0.023
-Yes	172 (90.1%)	140 (92.7%)	32 (80%)	
-No	19 (9.9%)	11 (7.3%)	8 (20%)	

Abbreviations: ASA, American society of anesthesia; BMI, Body mass index; NLR, Neutrophil to lymphocyte ratio; PLR, Platelet to lymphocyte ratio; PNL, Percutaneous nephrolithotomy; SWL, Shock Wave Lithotripsy.

without preoperative abdominal computed tomography (CT) images were excluded from the study.

A detailed medical history was obtained from all patients, and a physical examination, urinalysis, urine culture, blood count, and serum biochemical and coagulation tests were performed. Patients whose urine cultures demonstrated bacterial growth were treated preoperatively. Prophylactic antibiotic therapy (ciprofloxacin, 400 mg/200 ml twice daily) was maintained until the nephrostomy catheter was removed. Demographic and clinical data, including age, sex, body mass index, American Society of Anesthesiologists score, stone size and location, width of the renal parenchyma, preoperative NLR and PLR, fluoroscopy time, decrease in hemoglobin, stone-free status, and complication rate were analyzed in both groups. All patients were evaluated preoperatively with CT scan. Stone size was calculated by multiplying the maximum length and width of each stone and expressed in mm^2. Complications were evaluated based on the Clavien classification. Vital signs were monitored closely, and blood counts were performed postoperatively.

The presence of SIRS was determined based on the 2001 International Sepsis Definition Conference criteria.[11] Patients were diagnosed with SIRS when two or more of the following criteria were met: body temperature of < 36°C or > 38°C, heart rate of > 90 bpm, respiratory rate of > 20 breaths/min or PaCO2of < 32 mmHg and white blood cell count of > 12,000/mm3 or < 4,000/mm^3.

Procedures

An open-ended 6-Fr ureteral catheter was inserted with the aid of a rigid cystoscope with the patient in the lithotomy position under spinal anesthesia. The patient was then laid in the prone position, and radio-opaque material was inserted through the ureteral catheter using a C-arm fluoroscope. Intrarenal access was gained safely with an 18-G needle inserted through the appropriate calyx. After the guidewire had entered the collecting system, the access tract was dilated to 30-Fr with an amplatz dilators. A 26-Fr nephroscope was inserted into the kidney, and the stones were fragmented with a pneumatic lithotripter and extracted with stone forceps. The presence or absence of residual fragments was determined with a fluoroscope, and a tubeless nephrolithotomy was performed as indicated in: patients who have stone burden <3 cm, single tract access, no significant residual stones, no significant perforation, minimal bleeding, and no requirement for a secondary procedure.

After the procedure, the nephrostomy catheter was removed on postoperative day 1 to 3. If no hematuria was present, the ureteral catheter was removed the next day, and the patient was discharged. Otherwise, the implanted double-J stent was removed on postoperative day 15. The patients were evaluated on postoperative day 1

Table 2. Multivariate analysis for predicting systemic inflammatory response syndrome after percutaneous nephrolithotomy.

	P	Odds ratio	B	95%CI*
Preoperativ PLR ratio	0,018	1,01	0,012	1,002-1,022
Access number	0,026	0,221	1,508	0,058-0,838

Abbreviations: CI, confidence interval; PLR, Platelet-to-Lymphocyte Ratio

with a kidney, ureter, and bladder X-rays (KUB) and biochemical tests. The final stone-free rate was evaluated using ultrasound, KUB, or CT.

Statistical analysis

SPSS ver. 21 software (IBM Corp., Armonk, NY, USA) was used for the statistical analysis. Numerical data are expressed as mean ± standard deviation, and categorical data are indicated as numbers and percentages. The chi-square test was used to analyze categorical variables, and the independent sample t-test was used for numerical variables. A *P*-value of < .05 was considered statistically significant. Variables significant in the univariate analysis were evaluated using a multiple logistic regression model to determine the independent risk factors for developing SIRS after PNL. Adjusted odd ratios and 95% confidence intervals were calculated. A receiver operating characteristic (ROC) curve was constructed, and a cut-off value for the preoperative PLR was determined.

RESULTS

A total of 192 patients (131 male, 61 female) were included in the study. SIRS developed postoperatively in 41 (21.3%) patients. The mean age of the patients was 47.3 ± 15.1 years (range, 18 – 81 years), and the mean body mass index was 28.5 ± 5.1 kg/m2 (range, 18.0 – 47.9 kg/m2). The mean stone size was 675.9 ± 619.1 mm2 (range, 90 – 3800 mm2). The mean PLR was 116.7 ± 39.9 (range, 55 – 350), and the mean NLR was 2.6 ± 1.5 (range, 1 – 16). A total of 56 (29.1%) patients had previously undergone shock wave lithotripsy, PNL, or open surgery for renal stones. The mean operative time was 52.0 ± 31.8 min (range, 15 – 180 min). A single access site (n = 175; 91.1%) or multiple access sites (n = 17; 8.9%) were used to extract the stones, and the mean hospital duration was 1.88 ± 1.0 days (range, 1 – 7 days). Minor complications developed in 19 (11.7%) patients, and 5 patients (2.6%) developed major complications. Blood transfusion was required in 5 patients in group 1 and 3 patients in group 2. As a consequence, 156 (81.2%) patients were stone-free. Residual fragments measuring ≤ 4 and > 4 mm in diameter were detected in 16 (8.4%) and 20 (10.4%) cases, respectively. The patient demographic and operative data are shown in **Table 1**.

Univariate analysis revealed significant intergroup differences between the preoperative PLR and NLR, mean parenchymal thickness, number of access sites, operation duration, decrease in hemoglobin, presence of complications, and stone-free rate (*P* < 0.001, 0.018, .020, *P* < 0.001, *P* < 0.001, 0.016, 0.019, *P* < 0.001, and 0.023, respectively) (**Table 1**). Multivariate analysis showed that the preoperative PLR and number of access sites were independent factors affecting the postoperative development of SIRS (95% CI: 1.002-1.022, OR= 1.01, P = .018 and 95% CI: 0.058-0.838, OR = 0.221, *P* = .026, respectively) (**Table 1**). Preoperative NLR was revealed insignificant in multivariate analysis. The preoperative PLR cut-off value from the ROC analysis was 114.1, which had 80.4% sensitivity, 60.2% specificity, a 35.4% positive predictive value, and a 91.9% negative predictive value (**Table 2**). The area under the ROC curve was 73.1% (**Figure 1**).

DISCUSSION

PNL is a safe and effective minimally invasive method for managing renal stones, with a reported complication rate of 3% to 83%.[2,12] Sepsis is one of the more serious complications and is associated with higher mortality and morbidity rates. Some studies have reported that sepsis is the most frequent cause of perioperative mortality.[3,13] SIRS was first defined by Dr. William R. Nelson in 1983. Ischemia, inflammation, trauma, infection, or their combinations cause SIRS, which is closely related to sepsis. However, few studies have reported the development of SIRS after PNL.[10,14] The PLR and NLR are among the few hematological markers related to SIRS that increase in patients with SIRS. Many studies have reported that the PLR and NLR are closely associated with gastrointestinal and genitourinary system tumors.[5-8] A large-scale study of 27,000 patients by Proctor et al. demonstrated the importance of the PLR for predicting the outcomes of various cancers.[15] The reported incidence rate of post-PNL SIRS ranges from 16.7% to 27.4%, which is similar to our result (21.3%).[10,14,16-18] However, no consensus has been reached on the risk factors that predict post-PNL development of SIRS. Chen et al. performed a univariate analysis showing that operative time, stone size, presence of pyelocaliectasis, staghorn stones, number of

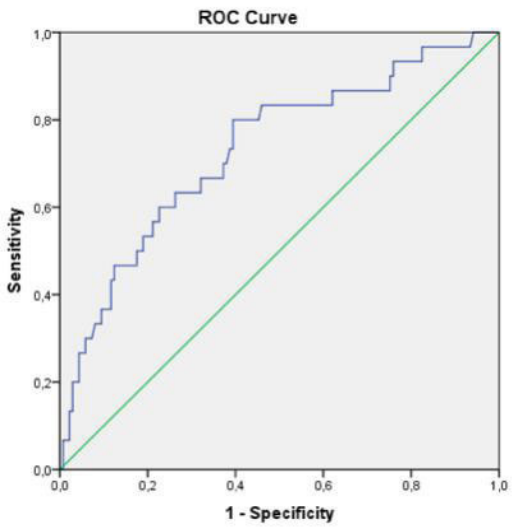

Figure 1. Receiver operating characteristic (ROC) curve analysis results of platelet to lymphocyte ratio.

access tracts, and blood transfusion were risk factors for the development of SIRS after PNL. However, their multivariate analysis demonstrated that blood transfusion, number of access tracts, stone size, and presence of pyelocaliectasis were independent predictive factors for the development of SIRS. According to their results, patients with these risk factors have a > 20-fold increased risk for developing SIRS.[14] In contrast, Erdil et al. reported that the results of pre- and intraoperative urine and stone cultures predicted the development of SIRS after PNL; no other factors were significant. The authors attributed this result to the strict criteria applied and stringent implementation of a preoperative antibiotic regimen.[10]

Our univariate analysis showed that the preoperative PLR and NLR, mean parenchymal thickness, number of access sites, operative time, decrease in hemoglobin, presence of complications, and stone-free rate were related to the development of SIRS. Similar to our results, Gutierrez et al. concluded that the presence of residual stone fragments is related to postoperative fever, whereas Draga et al. and Erdil et al. found no association among residual stones, postoperative fever, and SIRS.[9,10,19]

Although no study has demonstrated an association between renal parenchymal thickness and SIRS, Tepeler et al. reported a correlation between increased renal parenchyma thickness and a postoperative drop in hemoglobin.[20] Based on this conclusion, the injury caused by PNL performed in patients with a thicker renal parenchyma is more severe, increases the risk of SIRS, and results in more bleeding than in patients with a thinner renal parenchyma.

Studies based on the Clavien classification have reported that SIRS is associated with complications. Indeed, a frequently observed post-PNL complication is fever, which is also a SIRS criterion. One of our patients who developed postoperative fever with subsequent sepsis recovered without sequelae.

Evaluations based on the number of access sites have revealed that SIRS occurs more frequently in patients with multiple access sites than in patients with a single access site. In addition, multiple access sites are an independent risk factor for the development of SIRS. This result may be due to the increased trauma caused by multiple access sites, which enhances the systemic inflammatory response to trauma and may be responsible for the development of SIRS.

In addition to the factors analyzed to date, we have herein reported for the first time that the PLR and NLR are novel noninvasive biomarkers that predict post-PNL development of SIRS. However, only the PLR was statistically significant in the multivariate analysis. The preoperative PLR was higher in patients with than without SIRS. The PLR cut-off value of 114.1 resulted in 80.4% sensitivity, 60.2% specificity, a 35.4% positive predictive value, and a 91.9% negative predictive value.

Our study had some limitations. Because this study was retrospective, inflammatory markers such as C-reactive protein, interleukin-6, tumor necrosis factor-alpha, the sedimentation rate, and endotoxins were not evaluated. All of the patients were operated by two different urologists. In addition, intraoperative urine and stone cultures were not performed.

CONCLUSIONS

Predicting SIRS, which is associated with sepsis and other complications, is important for the physician and patient. Based on our findings, extreme care should be exercised in patients with a PLR of > 114.1 and multiple access sites because these patients have an increased probability of developing SIRS and should be followed up more closely. A preoperative PLR evaluation is a simple, cost-effective, and noninvasive test with which to predict the development of SIRS. Further prospective randomized studies are required compare PLR, NLR, access number and other parameter.

CONFLICT OF INTEREST

No conflicts of interest are declared by the authors.

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