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Can Preoperative Neutrophil-Lymphocyte Ratio and Platelet-Lymphocyte Ratio Predict Systemic Inflammatory Response Syndrome That Develops After Percutaneous Nephrolithotomy?

Preoperatif Nötrofil-Lenfosit Oranı ve Trombosit-Lenfosit Oranı, Perkütan Nefrolitotomi Sonrası Gelişen Sistemik Inflamatuar Yanıt Sendromunu Öngörebilir mi?

Özgün Araştırma
Research Article

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ABSTRACT

Objective: *First objective of this study was to find out factors influencing development of postoperative systemic inflammatory response syndrome (SIRS) after percutaneous nephrolithotomy (PNL). Secondary objective was to point out the role of preoperative neutrophil-lymphocyte ratio (NLR) and platelet-lymphocyte ratio (PLR) in SIRS estimation.*
Method: *The data of 756 patients that underwent PNL for kidney stones between 2012 and 2019 were evaluated retrospectively. Patients were divided into 2 groups as non-SIRS and SIRS group. The effects of NLR, PLR and other operative and demographic variables on development of SIRS were investigated. Multivariate logistic regression analysis that was performed on variables that were significant in the univariate analyses was used to establish independent risk factor for post-PNL SIRS.*
Results: *Univariate analysis revealed a significant association between presence of SIRS and preoperative PLR (p<0.001), preoperative NLR (p<0.001), blood transfusion (p<0.001), stone volume (p=0.03), staghorn stone (p<0.001), and preoperative creatinine levels (<0.001). Multivariate logistic regression analyses of these risk factors showed that NLR (p<0.001), PLR (p<0.001), and blood transfusions (p<0.001) were independently associated with SIRS. When the cut-off value of PLR was 120.5, the development of SIRS was predicted with 80.1% specificity and 81% sensitivity. When the cut-off value of NLR was 2.75, the development of SIRS was predicted with 64% specificity and 63.7% sensitivity.*
Conclusion: *Preoperative PLR and NLR are effective and inexpensive biomarkers that can be used to predict SIRS and sepsis after PNL. We recommend that patients with PLR >120.5, NLR >2.75, and blood transfusions should be monitored closely due to the possible development of serious complications.*

Keywords: *Neutrophil lymphocyte ratio, platelet-lymphocyte ratio, systemic inflammatory response syndrome, percutaneous nephrolithotomy, sepsis*

ÖZ

Amaç: *Bu çalışmanın ilk amacı; perkütan nefrolitotomi (PNL) sonrası postoperatif sistemik inflamatuar yanıt sendromunun (SIRS) gelişimini etkileyen faktörleri ortaya koymaktır. İkincil amaç; SIRS gelişiminde preoperatif trombosit-lenfosit oranının (PLR) ve nötrofil-lenfosit oranının (NLR) rolünü belirlemektir.*
Yöntem: *Çalışmaya 2012-2019 yılları arasında böbrek taşları için PNL uygulanan ve verileri retrospektif toplanan 756 hasta dahil edildi. Hastalar SIRS olmayan (nonSIRS grup) ve SIRS olan (SIRS grup) grup olarak 2 ye ayrıldı. PLR, NLR, diğer demografik ve operatif verilerin SIRS gelişimini ürerine etkileri araştırıldı. Tek değişkenli analizde anlamlı çıkan değişkenler, PNL'den sonra SIRS gelişimi için bağımsız risk faktörlerini belirlemek amacıyla çoklu lojistik regresyon modeli kullanılarak değerlendirildi.*
Bulgular: *Tek değişkenli analiz SIRS grubu ile preoperatif PLR (P<,001), preoperatif NLR (P<0,001), kan transfüyonu (<0,001), taş volümü (p=0,03), staghorn taş (p<0,001) ve preoperatif kreatinin değeri (<0,001) parametreleri arasında istatistiksel anlamlı bir ilişki olduğunu ortaya koydu. Çok değişkenli lojistik regresyon analizleri NLR (p<0,001), PLR (p<0,001) ve kan transfüzyonu'nun (p<0,001), SIRS ile bağımsız olarak ilişkili olduğunu gösterdi. PLR'nin cut-off değeri 120,5 olarak alındığında, SIRS gelişimininin %81 duyarlılık ve %80,1 özgüllük ile tahmin edildiği, NLR'nin cut-off değeri 2,75 olarak alındığında SIRS gelişiminin %63,7 duyarlılık ve %64 özgüllük ile tahmin edildiği izlendi.*
Sonuç: *Preoperatif PLR ve NLR, PNL'den sonra SIRS ve sepsisi tahmin etmek için kullanılabilecek etkili ve ucuz biyobelirteçlerdir. Ciddi komplikasyonların olası gelişim ihtimaline karşın nedeniyle PLR> 120,5, NLR >2,75 olan kan transfüzyonu yapılan hastaları yakından izlenmesini önermekteyiz.*

Anahtar kelimeler: *Nötrofil lenfosit oranı, trombosit lenfosit oranı, sistemik inflamatuar yanıt sendromu, perkütan nefrolitotomi, sepsis*

INTRODUCTION

Percutaneous nephrolithotomy (PNL) is a minimally invasive highly successful technique recommended as the first-line treatment for kidney stones of ≥2 cm [1]. Despite its high success rates, PNL is associated with some complications. Sepsis is one of the most important complications and occurs in 0.3% to 3.1% of patients [2]. Reported mortality rates among those range from 25% to 50% [3,4].

Ischemic inflammatory response syndrome (SIRS), characterized by both infectious and non-infectious inflammation, is closely associated with the development of sepsis. Some studies have investigated the factors affecting the development of SIRS and febrile status after PNL [5-8]. Platelet-lymphocyte ratio (PLR) and neutrophil-lymphocyte ratio (NLR) are biomarkers that increase during inflammation [5,6,9]. Both PLR and NLR have been reported to be promising biomarkers in predicting prognosis and diagnosis in varied inflammatory response cancers and diseases [9]. Moreover, it has been reported that patients with kidney stones have higher NLR and PLR rates compared to those without kidney stones [9].

The literature examining the effect of NLR and PLR on the development of SIRS after PNL is quite limited [5,9]. In this study, we aimed to investigate whether preoperative PLR and NLR could be used as effective inflammatory markers in predicting the occurrence of SIRS after PNL.

MATERIAL and METHODS

After approval of the local ethics committee, medical records of 1011 patients that underwent PNL operation in our clinic between 2012 and 2019 were retrospectively reviewed. Nurse observations were also evaluated. Patients under 18 years of age, patients that had any SIRS criteria during preoperative evaluation, patients with previous nephrostomy tube or urinary stent placement, patients with oncological disease, those who underwent simultaneous ipsilateral or contralateral ureteroscopic intervention or bilateral PNL, patients that didn't have preoperative abdominal computed tomography (CT) images, and those with positive urine culture and any missing data were excluded from the study. A total of 756 patients were included in the study. The patients were divided into 2 groups depending on whether they developed SIRS postoperatively: non-SIRS group (n=577) and SIRS group (n=179). SIRS was defined as the presence of any two of these criteria: body temperature <36°C or >38°C, heart rate >90 bpm, respiratory rate >20 breaths/minute, $PaCO_2$ of <32 mmHg and white blood cell (leukocyte) count >12.000/mm^3 or <4.000/mm^3, and more than 10% immature forms [10].

Demographic and clinical data such as detailed medical histories and physical examinations, urinalysis, urine culture, complete blood count, serum biochemical values, American Society of Anesthesiology (ASA) score, stone size and location, preoperative NLR and PLR rates, decrease in hemoglobin, blood transfusion status, stone-free rate, and complication rates were analyzed in both groups. Complications were evaluated according to the Clavien classification. Patients were defined as stone-free if they didn't have any renal stones in the postoperative fluoroscopic imaging and 1st month tomography.

Surgical Procedure

After administering general anesthesia, all patients were placed in the lithotomy position and 6-Fr catheter was placed in the ureter under cystoscopic guidance. Then, patients were switched to prone position. The ureter catheter was used to inject an opaque material and calyx suitable for access was identified with fluoroscope. Then, the guiding catheter was inserted following the insertion of 18-gauge metal needle. Based on the single-step method, 6-Fr amplatz dilator was used to dilate the entry route, which was further dilated with 28-30 Fr amplatz dilator. The stone was reached with 24 Fr nephroscope and was broken with an ultrasonic lithotripter. At the end of the surgery, a 14 Fr malecot catheter was placed in some patients if they had residue or bleeding. This catheter was removed at the postoperative 1st to 3rd day.

Statistical analysis:

Comparison of categorical variables was performed by Pearson chi-square test and the Z-test was utilized for the others after Bonferroni method correction. Normality of the data was analyzed using the Kolmogorov-Smirnov test. For descriptive statistics, continuous variables with normal distribution were presented as mean±standard deviation and the variables fitting the normal distribution were evaluated by the Student's t-test. Likelihood of a type I error was considered α=0.05 for all tests. In addition, we performed univariate and multivariate logistic regression analysis to calculate odds ratio (OR) and 95% confidence interval (CI) to identify risk factors predicting SIRS following PNL. Receiver operating characteristic (ROC) was used to evaluate the cut-off points of PLR and NLR values. Statistical analyses were performed using the IBM SPSS V22 packaged software program.

RESULTS

A total of 756 patients were included in the study. The non-SIRS group consisted of 577 patients and the SIRS group had 179 patients. Postoperative SIRS rate was 23.6%, while the total sepsis rate was 1.5%. The mean age of the patients was 48.6±13.6 years. The mean stone size was 646.8±686 mm^2. The mean PLR was 115.6±21.6, and the mean NLR was 2.6±0.8. There was a significant difference between the groups in terms of stone location (staghorn stone), stone volume, preoperative creatinine level, creatinine change, NLR, PLR, and blood transfusion parameters (p<0.05). The rate of total complications and sepsis was higher in the SIRS group (p<0.05). The demographic characteristics and comparative p values of the groups are summarized in Table 1.

Binary logistic regression analysis was used to determine independent risk factors for SIRS. Univariate analysis revealed a statistical association between SIRS and preoperative PLR (p<0.001), preoperative NLR (p<0.001), blood transfusions (<0.001), stone volume (p=0.03), staghorn stones (p<0.001), and preoperative creatinine values (<0.001). Multivariate logistic regression analyses of the risk factors that were shown to be significant in the univariate regression analyses revealed that NLR (95% Confidence Interval (CI): 1.67-2.85, odds ratio (OR)=2.18, p<0.001), PLR (95% CI: 1.07-1.10, OR=1.08, p<0.001), and blood transfusions (95% CI: 1.35-5.02, OR=2.61, p<0.001) were independently associated with SIRS (Table 2).

Table 1. The groups' demographic characteristics and comparative p values.

	SIRS group (n=577)	Non SIRS group (n=179)	P value
Age	48.4±13.4	49.5±14.2	0.358
Gender. n (%)			0.607
Female	199 (34.5)	58 (32.4)	
Male	378 (65.5)	121 (67.6)	
ASA. n (%)			0.412
1	382 (66.2)	109 (60.9)	
2	175 (30.3)	62 (34.6)	
3	20 (3.5)	8 (4.5)	
Side (right/left)	251/326	78/101	0.986
Stone localization. n (%)			<0.001^{Z}
Calyx	225 (39)	32 (17.9)	
Renal pelvis	236 (40.9)	78 (43.6)	
Staghorn	116 (20.1)	69 (38.5)	
Stone size. mm	27.3±12.1	25.9±10.8	0.165
Stone volume. mm^2	615.8±682.9	747.0±691.8	0.027
HU	1022±329	1022±333	0.999
Stone-skin distance. mm	93.5±19.8	95.9±17.2	0.160
ESWL history	191 (33.1)	65 (36.3)	0.428
Surgical history. n (%)			0.108
Absent	420 (72.8)	142 (79.3)	
URS	75 (13)	22 (12.3)	
PNL	82 (14.2)	15 (8.4)	
Intercostal access. n (%)	27 (4.7)	9 (5.1)	0.837
Preoperative creatinine	1.01±0.22	1.09±0.34	0.001
Creatinine change	0.017±0.159	0.074±0.227	<0.001
Number of renal accesses	1.2±0.4	1.2±0.4	0.411
Operation time. min	111.0±38.6	116.2±44.1	0.124
Nephrostomy placement. n (%)	372 (64.5)	118 (65.9)	0.723
Catheter duration. days	1.1±0.4	1.1±0.5	0.978
NLR	2.5±0.8	3.1±1.0	<0.001
PLR	108.8±16.0	137.7±22.7	<0.001
Hemoglobin drop (g/dL)	1.7±1.3	1.9±1.4	0.117
Blood transfusions. n (%)	46 (8)	34 (19)	<0.001
Stone free rate. n (%)	393 (68.1)	122 (68.2)	0.991
Sepsis. n (%)	6 (1)	8 (4.5)	0.003
Clavien-Dindo score. n (%)			0.006
C1	67 (11.6)	18 (10.1)	
C2	82 (14.2)	41 (22.9)	
C3a	5 (0.9)	3 (1.7)	
C3b	5 (0.9)	2 (1.1)	
C4a	4 (0.7)	4 (2.2)	
C4b	1 (0.2)	3 (1.7)	
C5	1 (0.2)	1 (0.6)	
Complications. n (%)			0.006
Minor (C1-2)	561 (97.2)	166 (92.7)	
Major (C3-5)	16 (2.8)	13 (7.3)	
Length of hospital stay (day)	2.3±1.8	2.3±1.5	0.788

^{Z}: Z-test

ASA, American Society of Anesthesiologists; HU, Hounsefield Unit; PNL, percutaneous nephrolithotomy; URS, ureteroscopy; ESWL, Extra Corporeal Shock Wave Lithotripsy; NLR, neutrophil-lymphocyte ratio; PLR, platelet-lymphocyte ratio (PLR).

Table 2. Multivariate logistic regression analysis of risk factors predicting the development of SIRS after PNL.

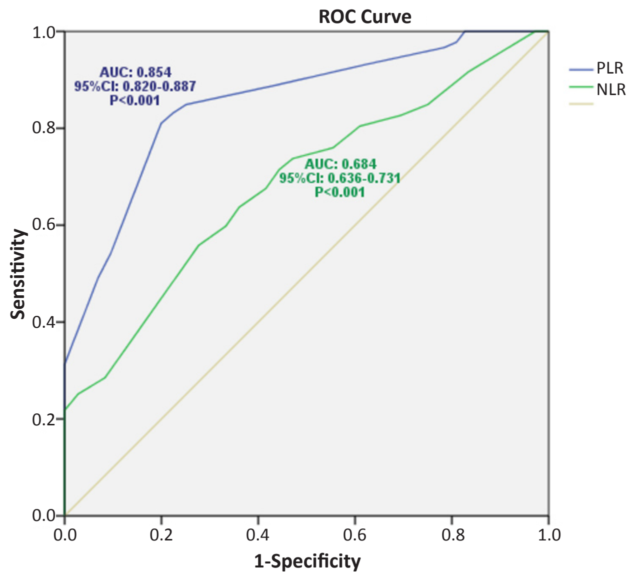
Binary Logistic Regression (n=756)	Univariate Model			Multivariate Model		
	OR	95% CI	P value	OR	95% CI	P value
Age	1.006	0.993 - 1.018	0.357			
Gender	0.911	0.637 - 1.301	0.607			
ASA	1.218	0.909 - 1.631	0.187			
Staghorn stone	2.493	1.733 - 3.585	**<0.001**			
Stone size	0.989	0.975 - 1.004	0.165			
Stone volume	1.000247	1.000024 - 1.000470	**0.030**			
ESWL history	1.152	0.812 - 1.636	0.428			
Surgical history	0.761	0.585 - 0.989	**0.041**			
Preoperatif kreatinin değeri	2.767	1.501 - 5.099	**0.001**			
Preoperative creatinine	1.003	0.999 - 1.007	0.124			
Number of renal accesses	0.844	0.563 - 1.264	0.411			
NLR	2.460	1.974 - 3.067	**<0.001**	2.186	1.674 - 2.855	**<0.001**
PLR	1.090	1.075 - 1.106	**<0.001**	1.088	1.072 - 1.104	**<0.001**
Hemoglobin drop	1.103	0.976 - 1.248	0.117			
Blood transfusion	2.707	1.675 - 4.373	**<0.001**	2.612	1.358 - 5.023	**<0.001**
Stone free rate	0.998	0.696 - 1.430	0.991			

ASA, American Society of Anesthesiologists; HU, Hounsefield Unit; PNL, percutaneous nephrolithotomy; URS, ureteroscopy; ESWL, Extra Corporeal Shock Wave Lithotripsy; NLR, neutrophil-lymphocyte ratio; PLR, platelet-lymphocyte ratio (PLR).

ROC curve analysis showed that PLR and NLR had predictive value for SIRS following PNL. The area under ROC curve (AUC) was 0.854 [95% confidence interval (95% CI)=0.820-0.887, p<0.001]. ROC curve analysis provided a PLR value of 120.5 as a cut-off point for postoperative SIRS development (sensitivity=81%, specificity=80.1%).

The AUC was 0.684 [95% confidence interval (95% CI)=0.636-0.731, p<0.001, Figure 1] and ROC curve analysis provided a NLR value of 2.75-value as a cut-off point for postoperative SIRS development (sensitivity=63.7%, specificity=64%).

Patients that are at risk for developing SIRS after PNL could be identified by using cut-off points of 120.5 and 2.75 for PLR and NLR, respectively. Considering the sensitivity, specificity and predictive values, it was determined that PLR was a more valuable predictor for SIRS.



Diagonal segments are produced by ties.

Figure 1. Details of the receiver operating characteristics (ROC) analysis of the effect of the PLR and NLR on postoperative SIRS after PNL.

DISCUSSION

PNL is a effective and safe minimally invasive technique used in the treatment of kidney stones. There are studies reporting complication rates between 3% and 83% [2,11]. Serious infections that cause severe sepsis and septic shock are unusual, but if they do occur, they can be destructive [2]. Sepsis is the most common cause of perioperative mortality [3,12].

It is known that ischemia, inflammation, trauma, infection or their combination may cause SIRS, which is closely related with sepsis [5-8]. NLR has been suggested as an infectious marker in sepsis and it has been found to be associated with severity of disease [13]. Gürol et al. [14] emphasized that the cut off value of 5 for NLR is quite successful in predicting sepsis and bacteremia. Many studies have reported that PLR and NLR are closely related with gastrointestinal and genitourinary system tumors [15-18]. Proctor et al.'s [19] large-scale study that evaluated 27,000 patients reported that PLR was effective in foreseeing the results of numerous types of cancers. However, there are limited studies investigating the occurrence of SIRS after PNL [8,20], and both PLR and NLR rates were reported in very few of these studies [5,9].

Operative time, stone burden, access number, and blood transfusion have been reported to be predictors of SIRS or postoperative fever [5,20-22]. According to Chen et al., [20] the significant risk factors for development of SIRS after PNL are blood transfusion, number of tracts, pyelocaliectasis, and stone size, however NLR or PLR were not evaluated. They reported that presence of these risk factors was associated with more than 20-fold increase in the SIRS development [20]. In a study examining the relationship between NLR and sepsis, the percentage of sepsis was significantly higher in the group with NLR ≥2.50 compared to the group with NLR <2.50 [6]. Çetinkaya et al. [5] reported that preoperative PLR is an inexpensive and effective biomarker to foresee SIRS after PNL. They recommended that patients with a PLR> 114.1 should be closely monitored due to the possibility of serious complications. The same study showed that preoperative PLR and NLR were associated with the development of SIRS [5]. Another study stated that NLR is an independent predictive factor for post-PNL SIRS, while PLR rate was also significantly higher in the group with SIRS [9].

Similar to the literature, the results of our study showed that staghorn stone, increased blood transfusion, stone volume, NLR, and PLR were associated with postoperative SIRS [5,6,9,20-22]. In addition, this is the first study that showed that high preoperative creatinine level and higher rate of increase in postoperative creatinine level were associated with the development of SIRS. Previous studies have shown that serum creatinine level was higher, albeit not significantly, in patients who developed SIRS after PNL [9]. We think that the higher creatinine level might have triggered systemic inflammation in some way. The results of our study did not reveal a relationship between operation time, number of accesses and SIRS.

Multivariate logistic regression analyzes showed that NLR, PLR, and blood transfusion were independently associated with SIRS. ROC curve analysis determined the NLR value of 120.5 (sensitivity=81%, specificity= 80.1%) and PLR value of 2.75 (sensitivity=63.7%, specificity=64%) as cut-off points for predicting postoperative SIRS. Our rates of SIRS development after PNL (23.6%) were similar to the studies in the literature that reported rates ranging between 16.7% and 27.4%. Our results also showed that sepsis was seen at a significantly higher rate in the SIRS group (non-SIRS 1%, SIRS group 4.5%).

In addition to the factors analyzed in previous studies, here we report that PLR and NLR can predictor SIRS development after PNL. To the best of our knowledge, this is the third study on this subject and the study with the highest sample size. Its retrospective design is the primary limitation of our study. Therefore, inflammatory markers such as interleukin-6, C-reactive protein, tumor necrosis factor-alpha and sedimentation could not be evaluated. In addition, not performing intraoperative urinalyses and stone culture and lack of stone analyses are other limitations.

CONCLUSION

Prediction of SIRS, which may be associated with sepsis and other complications, is important for both the patient and the physician. Based on our findings, we recommend that patients with PLR >120.5, NLR >2.75, and those who underwent blood transfusion should be followed up closely and carefully in the postoperative period. These markers are basic, easily measurable, and effortless to use in diurnal praxis at no extra cost. However, more exhaustive prospective studies are required to backing the findings of our study.

Ethics Committee Approval: S.B.U. Tepecik Training and Research Hospital Clinical Research Ethics Committee approval was obtained (Institutional review board approval number: 2021/03-01).

Conflict of Interest: All authors declare that there is no confict of interest.

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