DOI: https://doi.org/10.53350/pjmhs20221612912

ORIGINAL ARTICLE

Assessing the Preoperative Neutrophil-Lymphocyte Count Ratio's Predictive Ability for Postoperative Sepsis in Percutaneous Nephrolithotomy Patients

SHARIQ BIN YOUSUF[1], BAZGHA HASSAN[1], SHUAH ULLAH[1], LARAIB GUL[1], BILAL MASOOD KHAN[2], ASAD SHAHZAD HASSAN[3]
[1]FCPS, Lecturer, Department of Urology, Sindh Institute of Urology and Transplantation, Karachi, Pakistan
[2]FCPS, Asst. Professor Urology, Department of Urology, Sindh Institute of Urology and Transplantation, Karachi, Pakistan
[3]FCPS, Professor, Department of Urology, Sindh Institute of Urology and Transplantation, Karachi, Pakistan
Corresponding author: Shuah Ullah, Email: drsham084@gmail.com, Cell: +92 333 3020602

ABSTRACT

Background: The present study aimed to evaluate whether neutrophil lymphocyte count ratio (NLCR) can be used to detect post- PCNL sepsis.The objective of this study was to assess the potential of neutrophil-lymphocyte count ratio (NLCR) in detecting post-percutaneous nephrolithotomy (PCNL) sepsis.

Methodology: The Department of Urology, Sindh Institute of Urology and Transplantation, Karachi, conducted a cross-sectional study between 05-Oct-2019 to 04-April-2020. Patients of renal stone planned for PCNL, All adult patients of age 18-65 years, irrespective of gender, those with the preoperative total leukocyte count of between 4 and 12 x109 cells/L, and those patients with ASA class 1 were made to take part in the study. After involving the patients in the study, CT KUB was used to calculate stone size. Complete blood Count was done one week before PCNL and NLCR was calculated for all patients. After PCNL, patients were followed for 1 week. All the gathered information including demographic details (age, gender), preoperative findings (NLCR, Stone size, staghorn), intraoperative findings (operating time, tracts, blood transfusion) and postoperative findings (temperature, heart rate, respiratory rate, total leukocyte count, blood and urine cultures) was noted on a pre-designed Proforma.

Results: In this study, a total of 256 patients with a mean age of 41.17±10.18 years and a mean stone size of 29.1±6.3 mm were evaluated. The patients' mean operative time was 62.28±8.85 minutes. The area under the curve (AUC) was 0.824 in the ROC analysis, with the ideal cut-off value of NLCR being 2.5. The sensitivity and specificity of NLCR in predicting sepsis after PCNL were 50.0% and 98.0%, respectively, while the positive predictive value (PPV) was 80% and the negative predictive value (NPV) was 95.02%. The diagnostic accuracy was found to be 94.1%.

Conclusion: The risk of sepsis following percutaneous nephrolithotomy (PCNL) can be predicted with success using a cut-off value of ≥2.5 for neutrophil-lymphocyte count ratio (NLCR). Moreover, it is a simple, cost-effective, and noninvasive test and readily available in hospital laboratories.

Keywords: neutrophil lymphocyte count ratio, sepsis, percutaneous nephrolithotomy

INTRODUCTION

Renal calculi are best treated with percutaneous nephrolithotomy (PCNL), which has undergone significant advancements since its introduction in the 1980s. The usual indications for PCNL are stones larger than 20 mm and staghorn.[1,2] PCNL attains stone free rates of upto 95%[1].In Asia, about 1%–19.1% of the population suffer from urolithiasis.[3]

Postoperative infection is one of the most common complication of the procedure, and postoperative sepsis is one of the most detrimental.[4] Several factors contributed, including the number of tracts used, the size of the stone, the duration of the operation, the presence of a staghorn stone, and the need for blood transfusion.[5,6] Sepsis is defined as the systemic inflammatory response (SIRS) to infection.[7] Sepsis mortality rate is still high both in developed and in developing countries. Numerous approaches have been utilized to examine SIRS and sepsis extensively, including the implementation of diverse diagnostic, prognostic, and monitoring systems to evaluate the progression of patients with sepsis.[8] The most widely studied biomarkers in patients with suspected bacterial sepsis are C-reactive protein (CRP) and procalcitonin (PCT).[9] The neutrophil-to-lymphocyte ratio (NLCR) is an easily accessible biological marker that has been reported to represent disease severity.[10] NLCR values were more strongly significant in patients with sepsis than the values of classical parameters; such as CRP, white cell counts and serum lactate.[11]

Assessing the risk factors associated with the development of infectious complications following PCNL is crucial. One potential parameter for predicting sepsis after PCNL is the neutrophil-to-lymphocyte count ratio (NLCR). Sen et al. conducted a study which found that an NLCR >2.5 could be a useful predictor of post-operative sepsis after PCNL. In their research, 9.8% of patients with an NLCR >2.5 experienced sepsis, while only 3.2% of those with an NLCR <2.5 did. The study authors concluded that an NLCR >2.5 is an excellent indicator of the risk of developing post-PCNL sepsis.[12]

Literature review came up with only one study that has been conducted to date to determine the association of pre-op NLCR on post PCNL sepsis. Although the prognostic value of NLCR in patients with inflammatory and malignant conditions has been extensively studied, its potential role in predicting the risk of infectious complications following PCNL has not been explored in depth. The objective of this study was to investigate the usefulness of NLCR as a tool for detecting the presence of post-PCNL sepsis. If NLCR is really found to be effective in determining post-op sepsis, then it can be implemented as a routine method in pre-op period to prevent post- PCNL infections so that surgery can be delayed in these patients to prevent further morbidity and mortality due to infections.

METHODS AND MATERIALS

Between 05-Oct-2019 and 04-April-2020, a cross-sectional study was conducted at the Department of Urology in the Sindh Institute of Urology and Transplantation, located in Karachi. A non-probability consecutive sampling technique was used to recruit the participants in the study. Patients of renal stone planned for PCNL, All adult patients of age 18-65 years, irrespective of gender, those with the preoperative total leukocyte count of between 4 and 12 x109 cells/L, and those patients with ASA class 1 were included in the study.

Patients unfit for general anesthesia, blood and urine culture positive patients, those with malignancy, immunosuppression, those with diabetes, pyonephrosis kidneys, those with patients with preoperative nephrostomy tube, pregnant patients, and those with bleeding disorders were omitted from the study.

Sample size was calculated using OPENEPI a calculated using diagnostic accuracy sample size calculator taking statistics for sensitivity as 87.5%19, specificity as 90%19. Prevalence of sepsis as 9.8%margin of error for sensitivity as 13.0% and for specificity as 3.9 % the calculated sample size came out to 256.

Formulae for accuracy indices were as follows:

Sensitivity: TP/(TP+FN) × 100
Specificity: TN/(TN+FP) × 100
Positive predictive value: TP/(TP+FP) × 100
Negative predictive value: TN/(TN+FN) × 100
Diagnostic accuracy: TP+TN/(TN+TP+FP+FN) × 100

This study enrolled 256 patients with renal stone disease who were referred for PCNL to the Department of Urology, following approval by both the Research Evaluation Unit of the College of Physicians and Surgeons of Pakistan and the SIUT Ethics Research Committee. Prior to their inclusion in the study, all patients provided informed consent.

After including the patients in study, CT KUB was used to calculate stone size. Complete blood Count was done one week before PCNL and NLCR was calculated for all patients.

PCNL was done in all patients by consultant urologists. Following PCNL, patients were monitored for a period of one week. The diagnostic criteria for sepsis were based on the presence of the following: fever (>38°C or <36°C), heart rate (>90 beats/min), leukocyte count (4000 or >12000), respiratory rate (>20 breaths/min), and documented evidence of infection by urine and blood cultures. To be diagnosed with sepsis, patients had to meet at least two of these criteria.[17,18] All the gathered information including demographic details (age, gender), preoperative findings (NLCR, Stone size, staghorn), intraoperative findings (operating time, tracts, blood transfusion) and postoperative findings (temperature, heart rate, respiratory rate, total leukocyte count, blood and urine cultures) was noted on a pre-designed Proforma. Confidentiality was maintained.

Data was analyzed using Spss. version 20. Mean and standard deviation was calculated for age, stone size, operating time, blood transfusion and NLCR. Frequency and percentages were calculated for gender, tract, staghorn, finding on NLCR and sepsis. To determine the diagnostic accuracy of NLCR in detecting sepsis after PCNL, a 2 × 2 table was employed to calculate the sensitivity, specificity, positive predictive value, negative predictive value, and overall diagnostic accuracy. The effects of potential confounding variables, such as age, gender, staghorn, stone size, operating time, and blood transfusion, were assessed using stratification. The results of the stratification analysis were used to generate a post-stratification 2 × 2 table, which was then used to calculate the diagnostic accuracy parameters. Additionally, a ROC curve was plotted to identify the optimal cut-off value for NLCR.

RESULTS

A total number of 256 patients were included in this study. Mean age of patients was 41.17±10.18 years. Minimum age was 18 years and maximum age was 65 years. Mean stone size of patients was 29.1±6.3 mm. Minimum stone size was 20 mm and maximum stone size was 40 mm. Mean operative time of patients was 62.28±8.85 mins. Minimum operative time was 47 mins and maximum operative time was 87 mins (Table 1).

Mean blood transfusion of patients was 0.059±0.27 pints. Blood transfusion was required in only 16 (6.2%) patients. There were only 2 patients in whom 2 pints of blood were required, while in 14 patients only 1 pint was needed Mean NLCR of patients was 2.10±0.22. Minimum NLCR was 1.50 and maximum NLCR was 3.00. There were more male as compared to female patients. There were 168 (65.63%) male patients and 88 (34.38%) female patients in this study. There were 214 (83.59%) patients diagnosed with single track versus 42 (16.41%) patients diagnosed with multiple track. Staghorn stone was diagnosed in 27 (10.55%) patients while it was not diagnosed in 229 (89.45%) patients. On frequency of sepsis in NLCR, 24 (9.38%) patients were found with sepsis in NLCR versus 232 (90.62%) patients were not found in sepsis in NLCR. Sepsis was found in 15 (5.86%) Patients and it was not found in 241 (94.14%) patients (Table 2).

The ROC analysis showed that the area under the curve (AUC) was 0.824, and the optimal cut-off value for NLCR was determined to be 2.5 (as shown in Figure 1).

According to the results presented in Table 3, the sensitivity of NLCR in predicting sepsis after PCNL was 50.0%, while the specificity was 98.0%. The positive predictive value (PPV) was found to be 80%, and the negative predictive value (NPV) was 95.02%. The overall diagnostic accuracy of NLCR was 94.1%.

In patients having age >40 years, sensitivity of sepsis in NLCR was 80.0%, specificity 96.7%, PPV 66.7%, NPV 98.3% and diagnostic accuracy was 95.4%. In female patients, sensitivity of NLCR was 85.7%, specificity 95.1%, PPV 60.0%, NPV 98.7% and diagnostic accuracy was 94.3%. In patients having no staghorn stone, sensitivity of sepsis in NLCR was 72.7%, specificity 94.5%, PPV 40.0%, NPV 98.6% and diagnostic accuracy was 93.4% (Table 4).

Table 1: Patient Characteristics (Part I)

Parameters	Mean ± SD
Age (years)	41.17 ± 10.18
Stone Size (mm)	29.1 ± 6.3
Operative Time (minutes)	62.28 ± 8.85
Blood Transfusion (pints)	0.07 ± 0.28
NLCR	2.10 ± 0.22

Table 2: Patient Characteristics (Part II)

Parameters	Frequency N(%)
Gender	
Male	168(65.63%)
Female	88(34.38%)
Tract	
Single	214(83.59%)
Multiple	42(16.41%)
Staghorn stones	
Yes	27 (10.55%)
No	229 (89.45%)
Sepsis in NLCR	
Yes	24(9.38%)
No	232(90.63%)
Sepsis	
Yes	15(5.86%)
No	241(94.14%)

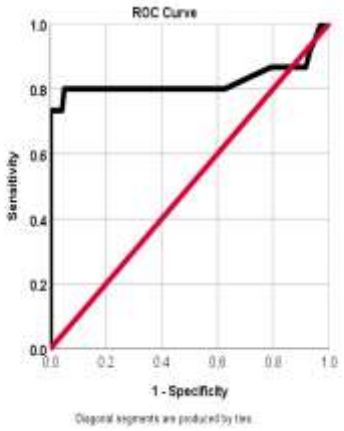

Figure 1: Area Under the Curve reflecting the sensitivity and specificity

Area Under the Curve:

Asymptotic 95% Confidence Interval
Test Result Variable(s): NLCR
Area 824
Std. Error[a] 090
Asymptotic Sig.[b] 000
Lower Bound 648
Upper Bound 1.000

The statistical analysis of the NLCR test results for predicting sepsis after PCNL may be biased due to the presence of ties in the test result variable between the positive and negative actual state groups.

A Under the nonparametric assumption
B Null hypothesis: true area = 0.5

Table 3: The diagnostic accuracy of NLCR in predicting sepsis after PCNL

		Sepsis in NLCR		Total
		Yes	No	
Sepsis	Yes	12	12	24
	No	03	229	232
Total		15	241	256

Table 4: Stratification of Age, Gender, (Staghorn stone = Yes/No), stone size, Operating Time (mins), Blood Transfusion (pints)

(Age Group 18-40 Years)				
		Sepsis in NLCR		Total
		Yes	No	
Sepsis	Yes	04	01	05
	No	08	112	120
Total		12	113	125
(Age Group 41-65 Years)				
		Sepsis in NLCR		Total
		Yes	No	
Sepsis	Yes	08	02	10
	No	04	117	121
Total		12	119	131
Males				
		Sepsis in NLCR		Total
		Yes	No	
Sepsis	Yes	06	02	08
	No	08	152	160
Total		14	154	168
Females				
		Sepsis in NLCR		Total
		Yes	No	
Sepsis	Yes	06	01	07
	No	04	77	81
Total		10	78	88
(Staghorn stone = Yes)				
		Sepsis in NLCR		Total
		Yes	No	
Sepsis	Yes	04	0	04
	No	0	23	23
Total		04	23	27
(Staghorn stone = No)				
		Sepsis in NLCR		Total
		Yes	No	
Sepsis	Yes	08	03	11
	No	12	206	218
Total		20	209	229
(Stone Size = 20.0-27.0 mm)				
		Sepsis in NLCR		Total
		Yes	No	
Sepsis	Yes	06	02	08
	No	03	112	115
Total		09	114	123
(Stone Size = 28.0-40.0 mm)				
		Sepsis in NLCR		Total
		Yes	No	
Sepsis	Yes	06	01	07
	No	09	117	126
Total		15	118	133
(Operating Time = 47-60 Minutes)				
		Sepsis in NLCR		Total
		Yes	No	
Sepsis	Yes	06	01	07
	No	08	123	131
Total		14	124	138
(Operating Time = 61-87 Minutes)				
		Sepsis in NLCR		Total
		Yes	No	
Sepsis	Yes	06	02	08
	No	04	106	110
Total		10	108	118
(Blood Transfusion = No Transfusion)				
		Sepsis in NLCR		Total
		Yes	No	
Sepsis	Yes	12	03	15
	No	11	214	225
Total		23	217	240
(Blood Transfusion = 1-2 Pint)				
		Sepsis in NLCR		Total
		Yes	No	
Sepsis	Yes	1	15	16
	No	1	15	16
Total		2	30	32

DISCUSSION

PCNL is generally a safe procedure with a low incidence of complications. However, fever and infectious complications are among the most frequently encountered issues. Postoperative fever has been reported in 10-25% of cases and is usually managed conservatively with a short course of intravenous antibiotics, leading to a complete recovery. [13] Nonetheless, the development of severe infections resulting in septic shock is a rare but potentially devastating complication that needs prompt recognition and treatment.[14]

According to O'Keeffe et al., severe sepsis occurred in 9 out of 700 patients who received percutaneous or endoscopic procedures for upper urinary tract stones, with a mortality rate of 66% in their series.[15] In a 1995 study examining its diagnostic value in appendicitis, Goodman et al. first introduced NLCR, proposing that it was a more sensitive measure than the total leukocyte count.[16] Several studies have further examined NLCR, and elevated NLCR values have been linked to unfavorable outcomes in patients with different types of cancer such as gastric cancer, prostate cancer, bladder cancer, colorectal cancer, renal cell carcinoma, and lung cancer.[17,18] NLCR has been proposed as a useful infection marker in patients with sepsis, and studies have shown a correlation between NLCR levels and disease severity.[19] According to Terradas et al., patients with bacteremia who had an NLCR greater than 7 had a higher risk of mortality, and this factor was identified as an independent marker.[20] De Jager et al. determined that NLCR was a more effective predictor of bacteremia than routine parameters such as C-reactive protein level, white blood cell count, or neutrophil count, using a cutoff point of 10.0 for NLCR.[21] In patients with Fournier's gangrene, an association was found between NLCR and increased mortality, the need for intensive care unit, and prolonged hospitalization times.[22] Gu¨rol et al. suggested that using a cutoff point of 5.0 for NLCR is more effective in predicting bacteremia and sepsis.[23]

Studies have investigated the potential molecular mechanisms underlying the correlation between NLCR and infectious complications (fever, SIRS, sepsis) as well as malignancies. These investigations have revealed that the plasma levels of proinflammatory cytokines, such as interleukin (IL)-1ra, IL-6, IL-7, IL-8, and IL-12, are elevated in patients with high NLCR.[24,25] The accumulation of these proinflammatory cytokines in the tissue microenvironment can lead to aggressive inflammation or tumor behavior. Moreover, elevated NLCR levels have been associated with high peritumoral infiltration by macrophages in cancer patients. The NLCR appears to be a useful marker for the upregulation of the innate immune response.

The NLCR has been hypothesized to accurately represent the underlying inflammatory process, with other hypotheses suggesting that the release of arachidonic acid metabolites and platelet-activating factors triggered by inflammation may result in neutrophilia, while cortisol-induced stress may lead to relative lymphopenia.[26]

A few studies have investigated the efficacy of preoperative NLCR in predicting postoperative complications. According to Yildirim et al., preoperative NLCR can serve as a predictive serum marker for the presence of tubo-ovarian abscess.[27]A correlation was observed between higher complication rates after major abdominal surgery and higher preoperative NLCRs, as reported by Forget et al.[28] Yanartas et al. conducted a study to investigate the potential of preoperative NLCR in predicting postoperative mortality in patients with chronic thromboembolic pulmonary hypertension. The study found that patients with high NLCR at admission had significantly higher mortality rates. The researchers also performed ROC analysis and identified a cutoff point of 2.54 for NLCR at admission, which was useful in predicting mortality. Moreover, the study demonstrated a significant correlation between preoperative pulmonary vascular resistance and NLCR, based on the correlation analysis.[29] Lee et al. found that a preoperative NLCR ≥3.0 was significantly correlated with severe cholecystitis and longer hospitalization in patients who underwent cholecystectomy. They concluded that NLCR may serve as a useful surrogate marker for severe cholecystitis.[30]

In the present study, we assessed the predictive value of NLCR in determining the risk of sepsis following PCNL. We found

that NLCR has a cut off value of ≥2.5. We found sensitivity of NLCR in predictive after NLCR was 80.0%, specificity was 95.0%, positive predictive value (PPV) was 50.0% and negative predictive value (NPV) was 98.7% and diagnostic accuracy was 94.1%.

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 a single urologist. In addition, intraoperative urine and stone cultures were not performed.

CONCLUSION

Neutrophil lymphocyte count ratio (NLCR) at a cut off value of ≥2.5 can successfully predict the risk of sepsis after percutaneous nephrolithotomy (PCNL). Moreover, it is a simple, cost-effective, and noninvasive test and readily available in hospital laboratories.

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