

Is Neutrophil / Lymphocyte Ratio Really Significant in Small Renal Masses?

Ibrahim Topçu* and Fatih Oğuz

Inonu University, School of Medicine, Department of Urology, Turkey

***Corresponding author:** Ibrahim Topçu, Department of Urology, Faculty of Medicine, Inonu University, 44280, Malatya, Turkey

ARTICLE INFO

Received: 📅 July 11, 2023

Published: 📅 July 21, 2023

Citation: Ibrahim Topçu and Fatih Oğuz. Is Neutrophil / Lymphocyte Ratio Really Significant in Small Renal Masses?. Biomed J Sci & Tech Res 51(4)-2023. BJSTR. MS.ID.008141.

ABSTRACT

Background: In this study, patients who underwent partial nephrectomy through the nephron sparing surgery for renal mass in our clinic were retrospectively screened. We aimed to evaluate patients by preoperative neutrophil to lymphocyte ratio incidence and the relation with PADUA scoring system, which is the widely used nephrometry score.

Material and Method: 51 patients and 52 renal masses were included into the study. Significance test was performed in terms of preoperative neutrophil to lymphocyte ratios, PADUA scores, bleeding quantities, pathological types, and histological grades.

Results: No statistically significant difference was found in the histological grade, pathologic type, PADUA score, preoperative neutrophil to lymphocyte ratios in the statistical comparison of patients with partial nephrectomy. Only age together with tumor size and preoperative neutrophil to lymphocyte ratio together with bleeding amount significantly correlated.

Conclusions: Partial nephrectomy is a technique that can be safely performed especially in T1 early-stage tumors. However, we think that preoperative neutrophil / lymphocyte ratio cannot be used as a prognostic factor in early-stage tumors.

Keywords: Partial Nephrectomy; Renal Mass; PADUA; Nephrometry Score; Neutrophil / Lymphocyte Ratio; NLR: Neutrophil/Lymphocyte Ratio

Abbreviations: RCC: Renal Cell Carcinomas; PN: Partia Nephrectomy; PADUA: Preoperative Aspects and Dimensions Used for an Anatomical; SPSS: Statistical Package for Social Sciences

Introduction

Renal tumors constitute 2-3% of all tumors in adulthood [1] and are more common in developed societies. Recently, the incidence of kidney tumors has been increasing with the more frequent use of imaging methods [2]. The most common renal tumors are Renal Cell Carcinomas (RCC), which constitutes approximately 85% of all kidney tumors [3]. Although 20-30% of patients with RCC are metastatic at the time of diagnosis, surgical intervention can be achieved in patients diagnosed at an early stage. However, metastases may occur in 20-40% of patients after surgery. Partial nephrectomy (PN) surgery is the recommended treatment method for T1a RCC [4], and some nephrometric scores have been developed to predict the complications that may occur in this surgical method and the prognosis of the

disease. Among these scores, the Preoperative Aspects and Dimensions Used for an Anatomical (PADUA) system is most frequently used [5]. Despite the recent popularity of molecular factors to predict prognosis, no better predictor of prognosis than tumor stage and tumor grade has not been found yet. For this reason, different prognostic factors are being investigated. Neutrophil/lymphocyte ratio (NLR) is shown as a candidate among these prognostic factors. The basic idea in investigating this factor is that systemic inflammation plays an important role in preventing tumor development and metastasis [6]. It is known that with a systemic inflammatory reaction, the number of neutrophils in the peripheral blood increases and the number of lymphocytes decreases [7]. From this point of view, when the prognostic factor related to the neutrophil/lymphocyte ratio was investigated, it was found to be significant for some solid tumors [8] such as melano-

ma [9], lung adenocarcinoma [10], bladder tumor [11]. However, research for RCC is conflicting. In this study, we thought that NLR might be effective in predicting the prognosis in small renal masses, and we aimed to present our results.

Materials and Methods

Patients who applied to the urology outpatient clinic with renal mass between September 2013 and March 2018 were retrospectively scanned. Patients who underwent surgical partial nephrectomy and whose data could be fully accessed were included in the study and the patients that underwent radical nephrectomy, active surveillance/palliative therapy, or whose data could not be fully accessed were excluded from the study (Figure 1). Demographic characteristics and laboratory findings of 51 patients and 52 renal units included in the

study were obtained by retrospective scanning in Mergentech v2.18 Program, which is the hospital information management system. Pre-operative images of kidney masses were obtained from the image archive of the Radiodiagnostics Department. During the evaluation, the side of the mass, its localization, its relationship with the renal sinus and collecting system, and surrounding tissues were examined, and PADUA scores were calculated. Pathological features were obtained from the pathology reports of the patients. Histological subtype, Fuhrman grade of the tumor, pathological size, condition of the surgical margin, tumor stage, sarcomatoid differentiation and coagulation necrosis were evaluated. The results were staged according to the 2017 TNM [12] staging, and the Fuhrman grading system was used for histological grading. Pathology results, PADUA scores and neutrophil lymphocyte ratios of the patients were evaluated by statistical significance.

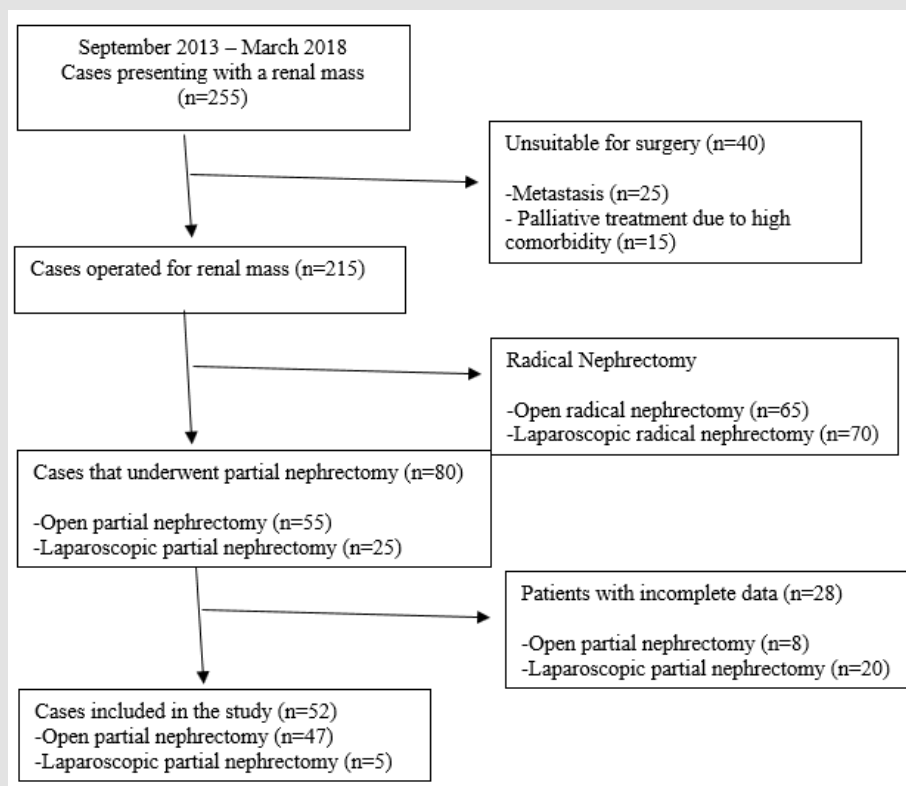


Figure 1: Flow-chart of the study.

Statistical Analysis

The analysis of all the obtained data was performed by saving it to the database created in the Windows Statistical Package for Social Sciences (SPSS v22.0) package program and taking the significance level as 0.05 at the 95% confidence interval. Conformity of continuous variables to normal distribution was investigated by Kolmogorov

Smirnov Test. Data conforming to normal distribution were evaluated with Student's t test, and data not conforming to the normal distribution were evaluated with Mann-Whitney U test. When evaluating dependent groups, those with normal distribution were analyzed with the t-test, and those that did not fit were analyzed with the Wilcoxon test. Statistical significance level was accepted as $p < 0.05$ in all analyzes.

Ethical Consent

In our study, written consent was obtained from all the cases participating in our study, in accordance with the Declaration of Helsinki. The study was approved by the Ethics Committee of İnönü University (Date: 04/09/2018, No: 2018/16-7).

Results

Table 1: Demographic Characteristics of the Patients.

	n (%)	P
M/F	33 (%64,7)/18 (%35,2)	-
Chronic Disease	28 (%54.9)	0.269
COPD/Asthma	6 (%21.4)	-
CAD	7 (%25)	-
DM	11 (%39.2)	-
Hypertension	17 (%60.7)	-
Hypothyroidism	4 (%14.2)	-
Smoking	15 (%29,4)	0.31
Operation Side		
Right	33 (%64.7)	-
Left	17 (%33.4)	-
Bilateral	1 (%1.96)	-
Complication	3 (%5,7)	-
Bleeding	2 (%66,7)	-
Urinary Extravasation	1 (%33,3)	-

Note: COPD: Chronic Obstructive Pulmonary Disease, CAD: Coronary Artery Disease, DM: Diabetes Mellitus.

Of the 51 patients included in the study, 33 were male and 18 were female, and the mean age was 55.54 (28-84) years. 28 patients had at least one chronic disease. Fifteen of the patients had a history of smoking. In the statistical analysis, there was no significant difference between the presence of chronic disease and smoking with Fuhrman grade (p: 0.621), tumor size (p: 0.125), NLR (p: 0.269), and PADUA score (p: 0.802). The demographic characteristics of the patients are summarized in Table 1. 33 of the patients had right, 17 had left and 1 had bilateral renal mass. Laparoscopic surgery was performed in 5 patients and open partial nephrectomy in 47 patients. There was no significant difference in terms of bleeding between the patients who underwent both methods (p: 0.379). The mean size of the masses was 40 mm (13-100 mm), and the mean volume was calculated as 26.8 mm³ (1.05-157.3 mm³). Tumors were divided into 3 groups according to their size as ≤ 4 cm, 4-7 cm and > 7 cm. Sarcomatoid dif-

ferentiation was not observed in any patient, but coagulation necrosis was positive in 5 patients and the mean NLR of these patients was calculated as 2.49, but it was not statistically significant (p: 0.662). Surgical margin was positive in 3 patients and their pathologies were clear cell RCC, papillary cell RCC type 1 and type 2. No local recurrence was observed in the follow-up of these patients. No significant difference was observed between the Fuhrman groups of tumors in terms of NLR. (p: 0.226). The pathological features of the patients are summarized in Table 2.

Table 2: Preoperative and Pathological Characteristics of the Tumor.

	n (%)	P
Tumor Stage		
T1a	26 (%50)	
T1b	24 (%46,1)	
T2a	2 (%3,9)	
Histological Classification	26 (%50)	
Clear Cell	11 (%21,1)	
Papillary Type -1	9 (%17,3)	
Papillary Type -2	6 (%11,5)	
Chromophobe	6 (%11,5)	
Fuhrman Grade*		
Low	39 (%84,8)	
High	7 (%15,2)	
Surgical Margin		0,226
Positive	3 (%5,7)	
Negative	49 (%94,3)	

Note: *Fuhrman 1 and 2 low, 3 and 4 high grade. Fuhrman was not calculated in the chromophobe cell cancer group.

The mean NLR of the patients was calculated as 2.70 (0.91-15.11). The mean PADUA score of the tumors was calculated as 8.5 (6-11). In the PADUA scoring system, when 6 and 7 were grouped as low risk (n=11) and 8 and above as high risk (n=49), the NLR cut-off value was calculated as 1.63 according to Youden-J index (0.2328). The specificity of this value was 81.82%, and the sensitivity was 41.46%. The area under the ROC curve was calculated as 0.548 (Figure 2). However, no significant correlation was found between NLR and PADUA score. The mean postoperative hemoglobin losses of the patients were calculated as 1.56 g/dl (-1.5 - 4.9). When the NLR ratio and the amount of bleeding were compared, it was statistically significant that the amount of bleeding increased as the value increased (p:0.038). Retroperitoneal

bleeding, a late complication, occurred in two of our patients and was controlled by angioembolization. Pseudoaneurysms were detected in both of their angiographies. Urine extravasation was also observed

in one of the patients and DJ stent was placed and followed up. After that, the defect closed and the DJ stent was removed 1 month later.

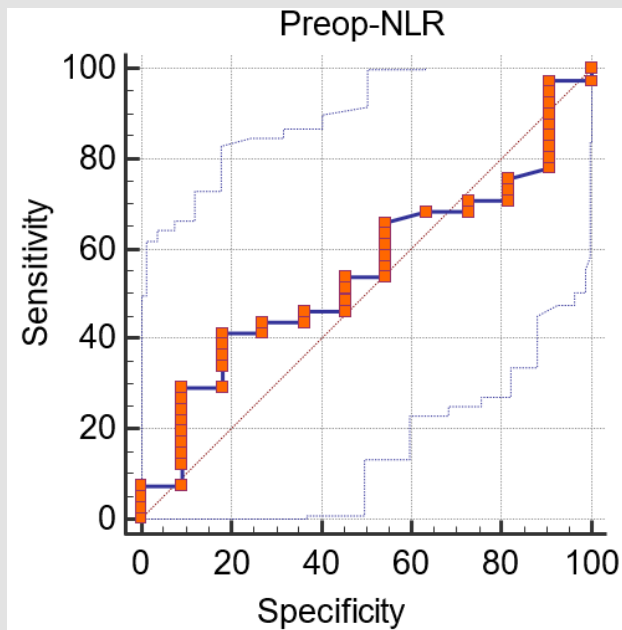


Figure 2: ROC curve of Neutrophil Leukocyte ratio by PADUA risk grouping.

Discussion

Renal Cell Carcinomas (RCC) are generally seen in the 5th-7th decades and are approximately 2 times more common in men than women [13]. In our study, the mean age at diagnosis was 55.54 (28-84) and the male/female ratio was 1.83, similar to the literature. Its etiology is multifactorial, the main ones are smoking, obesity and hypertension. There is also a genetic predisposition [14]. 28 patients had at least one chronic disease, and 24 patients did not have any chronic disease in our study. 15 patients had a history of smoking. However, there was no statistically significant result between the presence of chronic disease and NLR in our study. RCC consists of 4 main subtypes, but sarcomatoid differentiation and coagulation necrosis show a poor prognosis in all subtypes, regardless of the type [15]. In our study, the mean NLR of patients with positive coagulation necrosis was calculated as 2.49, and this value was not statistically significant when compared with other patients ($p: 0.662$). Fuhrman nuclear grading system is also a prognostic factor independent of histological subtype [16]. There are 4 categories in this system and the prognosis worsens as the degree increases. However, some studies argue that the Fuhrman rating system should be replaced with a 2- or 3-layer system [17-21]. When we evaluated our patients by grouping them according to the 2-layer grading system, there was no significant difference with NLR ($p: 0.226$). In a meta-analysis conducted on approximately 40,000

patients with solid tumors, it was found that cancer-specific survival was significantly reduced, and recurrence-free life was shortened in patients with a NLR above 4 as an indicator of the systemic inflammatory response [22].

In a study conducted by Wassim et al. in 2016, 1970 patients with clear cell RCC were investigated and it was found that NLR was significantly associated with overall survival, cancer-specific survival, and ASA score, but when prognostic factors were added to these results, the risk was not affected [23]. In another study conducted by Martino et al. on patients with non-clear cell RCC, the NLR significance ratio was calculated as 2.6, and it was shown that disease-free survival decreased by 15% for each 1-unit increase over 2.625. Otuncemur et al. evaluated 432 patients who underwent radical or partial nephrectomy for RCC and found that NLR increased significantly with the increase in tumor stage and histological grade [24]. In a study by Grgel et al., it was found that there was a significant difference in terms of neutrophil/lymphocyte ratios between patients with benign and malignant tumors in patients with localized RCC and therefore partial nephrectomy [25]. However, in these studies, patients who underwent partial nephrectomy and those with malignant tumors were not evaluated in terms of tumor stage and histological prognostic factors and the significance of NLR. In our study, the pathology of the patients who underwent partial nephrectomy and those with RCC were evalu-

ated within themselves. However, no statistically significant correlation was found between NLR and tumor stage, histological grade, and PADUA stage.

Conclusion

According to previous studies, NLR, which is an indicator of systemic inflammatory response, may be a prognostic factor in advanced solid tumors, but it is insufficient for its use in early-stage tumors. In our study, no significant correlation was found between NLR and PADUA score, so NLR should not be used as a prognostic factor in early stage RCC cases.

Conflict of Interest

The authors report no conflict of interest.

References

1. Van Poppel H (2004) Conservative vs radical surgery for renal cell carcinoma. *BJU international* 94(6): 766-768.
2. Hollingsworth JM, Miller DC, Daignault S, Hollenbeck BK (2006) Rising Incidence of Small Renal Masses: A Need to Reassess Treatment Effect. *JNCI: Journal of the National Cancer Institute* 98(18): 1331-1334.
3. Chow W, Devesa SS, Warren JL, Fraumeni, Jr JF (1999) Rising incidence of renal cell cancer in the United States. *JAMA* 281(17): 1628-1631.
4. Boulière F, Crepel M, Bigot P, Pignot G, Bessedé T, et al. (2011) Intérêt de la néphrectomie partielle pour la préservation de la fonction rénale des patients ayant une tumeur rénale de plus de 4cm. *Progrès en Urologie* 21(12): 842-850.
5. Ficarra V, Novara G, Secco S, Macchi V, Porzionato A, et al. (2009) Preoperative Aspects and Dimensions Used for an Anatomical (PADUA) Classification of Renal Tumours in Patients who are Candidates for Nephron-Sparing Surgery. *European Urology* 56(5): 786-793.
6. Grivennikov SI, Greten FR, Karin M (2010) Immunity, Inflammation, and Cancer. *Cell* 140(6): 883-899.
7. Zahorec R (2001) Ratio of neutrophil to lymphocyte counts-rapid and simple parameter of systemic inflammation and stress in critically ill. *Bratislavske lekarske listy* 102(1): 5-14.
8. Templeton AJ, McNamara MG, Šeruga B, Vera-Badillo FE, Aneja P, et al. (2014) Prognostic Role of Neutrophil-to-Lymphocyte Ratio in Solid Tumors: A Systematic Review and Meta-Analysis. *JNCI: Journal of the National Cancer Institute* 106(6): 124.
9. Zhan H, Ma JY, Jian QC (2018) Prognostic significance of pretreatment neutrophil-to-lymphocyte ratio in melanoma patients: A meta-analysis. *Clinica chimica acta* 484: 136-140.
10. Minami S, Ihara S, Kim SH, Yamamoto S, Komuta K (2018) Lymphocyte to Monocyte Ratio and Modified Glasgow Prognostic Score Predict Prognosis of Lung Adenocarcinoma Without Driver Mutation. *World journal of oncology* 9(1): 13-20.
11. Camtosun A, Celik H, Altintas R, Topcu I, Tasdemir C (2017) Does preoperative neutrophil-to-lymphocyte ratio have a value in predicting recurrence in bladder tumour after intravesical BCG treatment?. *Biomedical Research* 28(1): 36-40.
12. Gospodarowicz MK, Miller D, Groome PA, Greene FL, Logan PA, et al. (2004) The process for continuous improvement of the TNM classification. *Cancer* 100(1): 1-5.
13. Kovacs G (1993) Molecular differential pathology of renal cell tumours. *Histopathology* 22(1): 1-8.
14. Bergstrom A, Hsieh CC, Lindblad P, Lu CM, Cook NR, et al. (2001) Obesity and renal cell cancer--A quantitative review. *British journal of cancer* 85(7): 984-990.
15. Cangiano T, Liao J, Naitoh J, Dorey F, Figlin R, et al. (1999) Sarcomatoid renal cell carcinoma: biologic behavior, prognosis, and response to combined surgical resection and immunotherapy. *Journal of clinical oncology* 17(2): 523-528.
16. Lang H, Lindner V, de Fromont M, Molinie V, Letourneux H, et al. (2005) Multicenter determination of optimal interobserver agreement using the Fuhrman grading system for renal cell carcinoma: Assessment of 241 patients with > 15-year follow-up. *Cancer* 103(3): 625-629.
17. Rioux-Leclercq N, Karakiewicz PI, Trinh QD, Ficarra V, Cindolo L, et al. (2007) Prognostic ability of simplified nuclear grading of renal cell carcinoma. *Cancer* 109(5): 868-874.
18. Sun M, Lughezzani G, Jeldres C, Isbarn H, Shariat SF, et al. (2009) A proposal for reclassification of the Fuhrman grading system in patients with clear cell renal cell carcinoma. *Eur Urol* 56(5): 775-781.
19. Tsui K-H, Shvarts O, Smith RB, Figlin RA, Belldegrun A (2000) Prognostic indicators for renal cell carcinoma: a multivariate analysis of 643 patients using the revised 1997 TNM staging criteria. *The Journal of urology* 163(4): 1090-1095.
20. Medeiros LJ, Jones EC, Aizawa S, Aldape HC, Chevile JC, et al. (1997) Grading of renal cell carcinoma. *Cancer* 80(5): 990-991.
21. Delahunt B, Chevile JC, Martignoni G, Humphrey PA, Magi-Galluzzi C, et al. (2013) The International Society of Urological Pathology (ISUP) grading system for renal cell carcinoma and other prognostic parameters. *The American journal of surgical pathology* 37(10): 1490-1504.
22. Bazzi WM, Tin AL, Sjoberg DD, Bernstein M, Russo P (2016) The prognostic utility of preoperative neutrophil-to-lymphocyte ratio in localized clear cell renal cell carcinoma. *The Canadian journal of urology* 23(1): 8151-8154.
23. de Martino M, Pantuck AJ, Hofbauer S, Waldert M, Shariat SF, et al. (2013) Prognostic impact of preoperative neutrophil-to-lymphocyte ratio in localized nonclear cell renal cell carcinoma. *The Journal of urology* 190(6): 1999-2004.
24. Otunctemur A, Dursun M, Besiroglu H, Ozer K, Horsanali O, et al. (2016) Clinical Significance of Preoperative Neutrophil-to-Lymphocyte Ratio in Renal Cell Carcinoma. *International braz j urol* 42(4): 678-684.
25. Gorgel SN, Ozer K, Kose O, Dindar AS (2018) Can preoperative neutrophil lymphocyte ratio predict malignancy in patients undergoing partial nephrectomy because of renal mass? *International Brazilian Journal of Urology* 44(3): 461-466.

ISSN: 2574-1241

DOI: 10.26717/BJSTR.2023.51.008141

Ibrahim Topçu. Biomed J Sci & Tech Res



This work is licensed under Creative Commons Attribution 4.0 License

Submission Link: <https://biomedres.us/submit-manuscript.php>



Assets of Publishing with us

- Global archiving of articles
- Immediate, unrestricted online access
- Rigorous Peer Review Process
- Authors Retain Copyrights
- Unique DOI for all articles

<https://biomedres.us/>