The Controlling Nutritional Status (CONUT) Score as a Predictor of Local Recurrence in Patients Underwent Partial Nephrectomy Alongside the R.E.N.A.L. Nephrometry Score

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Purpose: This study aims to assess the utility of the CONUT (Controlling Nutritional Status) Score and R.E.N.A.L. (Renal Nephrometry Score) Score in predicting tumor recurrence in patients with kidney cancer. Additionally, we investigated which parameters contributed to these scores.

Materials and Methods: In total, 115 patients who underwent partial nephrectomy between January 2015 and August 2023 at a single tertiary center were enrolled. After the exclusion criteria, data from 88 patients were analyzed. Age, gender, body mass index (BMI), comorbidities (hypertension, diabetes), smoking status, tumor characteristics, CONUT Scores, and R.E.N.A.L. scores were retrospectively recorded. Statistical analyses were performed, and significant p was $p < 0.05$.

Results: The presence of diabetes and hypertension showed a statistically significant association with tumor recurrence ($p = 0.033$ and $p = 0.003$, respectively). A high BMI significantly increased the risk of recurrence ($p < 0.05$). There was a strong positive relationship between the high tumor stage and positive surgical margins with recurrence ($p < 0.001$). Patients with high R.E.N.A.L. Scores and high CONUT Scores had a higher risk of recurrence (42.1% and 8.7%, respectively), and this difference was statistically significant ($p < 0.001$).

Conclusion: CONUT and R.E.N.A.L. scores may be used to predict tumor recurrence after partial nephrectomy. Additionally, diabetes, hypertension, high BMI, and positive surgical margin rate might affect surgical success rate for recurrences. Clinicians should consider all these parameters and coring systems to gather more successful results after partial nephrectomy.

Keywords: CONUT score; partial nephrectomy; predictive; recurrent renal cell carcinoma; renal cancer; R.E.N.A.L. nephrometry score

INTRODUCTION

Kidney cancer, also known as renal cell carcinoma, is a malignant tumor that originates in the cells of the kidney. Renal cell carcinoma (RCC) constitutes approximately 3.8% of all new cancers and has an average age of diagnosis of 64 years. Approximately 85% of kidney tumors are RCC[1]. Smoking, obesity, and hypertension are recognized risk factors for the development of RCC [2]. Partial nephrectomy is a surgical procedure commonly used in the treatment of low-grade kidney cancer. It involves the removal of the tumor along with a portion of the kidney tissue surrounding[3]. This approach is preferred over radical nephrectomy, which involves the complete removal of the kidney, as it allows for the preservation of renal function and has been associated with better long-term outcomes in appropriate patients [4] The R.E.N.A.L Nephrometry Score is a valuable tool used in the context of partial nephrectomy, particularly in the field of urology[5] It plays a crucial role in assessing the complexity of renal tumors and guiding surgical treatment. The Renal Nephrometry Score, also known as the R.E.N.A.L. Score, is a scoring system that takes into account various anatomical factors related to renal tumors, was developed by Kutikov and Uzzo in 2009. It helps surgeons to evaluate and classify renal masses based on specific parameters, providing a standardized method for describing tumor complexity[6].

The R.E.N.A.L. Score consists of five components, each of which represents different anatomical features of the tumor and its relationship with the surrounding kidney tissue: R (Radius): This component assesses the size of the tumor and its proximity to the renal collecting system. Tumors located near the collecting system may be more challenging to remove while preserving renal function. E (Exophytic/Endophytic): It categorizes whether the tumor is predominantly exophytic (growing outward) or endophytic (growing inward) within the kidney. This distinction impacts surgical treatment. N (Nearness to Collecting System or Sinus): It evaluates how close the tumor is to critical structures like the renal collecting system and renal sinus. Tumors near these structures may be more complex to manage. A (Anterior/Posterior): This component considers the location of the tumor within the kidney, whether it is anterior or posterior. Tumor location affects the surgical approach. L (Location Relative to Polar Lines): It divides the kidney into upper and lower poles and determines the location of the tumor in relation to these poles. This helps in specifying the tumor's position within the kidney.

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Table 1. Assessment of Undernutrition Degree by CONUT

Parameter	Undernutrition Degree			
	Normal	Light	Moderate	Severe
Serum Albumin (g/dL)	3.5 – 4.5	3.0 – 3.49	2.5 – 2.9	< 2.5
Score	0	2	4	6
Total Lymphocytes/mL	> 1600	1200 - 1599	800 - 1199	< 800
Score	0	1	2	3
Cholesterol (mg/dL)	> 180	140 - 180	100 - 139	< 100
Score	0	1	2	3
Screening Total Score	0 - 1	2 - 4	5 - 8	9 - 12

The R.E.N.A.L. Score assigns numerical values to each of these components, and these values are summed to calculate an overall score for the renal tumor. The total score provides an objective assessment of the tumor's complexity, with higher scores indicating more intricate and challenging tumors[7]. The significance of the R.E.N.A.L. score lies in its ability to assist surgeons in decision-making when considering partial nephrectomy as a treatment option. It helps identify tumors amenable to nephron-sparing surgery, where only the tumor and a minimal amount of surrounding healthy tissue are removed, preserving as much kidney function as possible. Conversely, tumors with higher R.E.N.A.L. Scores may be indicative of more complex cases where a radical nephrectomy (complete removal of the kidney) might be necessary. Additionally, this scale is a logical tool in the field of urology, aiding surgeons in the assessment of renal tumors and the selection of the most appropriate surgical approach, ultimately contributing to better patient outcomes and kidney function preservation[6]. In the literature, various scoring systems are utilized to aid in the decision-making process for partial nephrectomy, particularly in cases of renal tumors[8-11]. However, it may be more efficient to use the R.E.N.A.L. score, which is more widely used and can be understood internationally. Nevertheless, it has been observed that when deciding on partial nephrectomy, only anatomical parameters are taken into account. It is considered that the inclusion of scoring systems that incorporate metabolic parameters alongside anatomical parameters may be more beneficial in predicting the prognosis of patients undergoing partial nephrectomy for renal masses.

The Controlling Nutritional Status (CONUT) score is a tool that assesses the nutritional status of patients based on three parameters: serum albumin levels, total lymphocyte count, and total cholesterol levels[12]. It was initially developed as a prognostic indicator for patients with colorectal cancer[13]. However, its utility has been demonstrated in various other malignancies, including gastric cancer, pancreatic cancer, and acute myeloid leukemia[14–16]. In clinical oncology practice, the CONUT score has been shown to be a valuable predictor of outcomes in cancer patients, and it is associated with overall survival, recurrence-free survival, in-hospital mortality, sepsis, length of stay, and postoperative complications[17–20]. The CONUT score provides valuable information about the nutritional and immune status of patients, which are important factors in cancer prognosis and treatment response[21]. The use of the CONUT Score in oncology has several advantages, such as being simple and easily calculable score that can be obtained from routine laboratory tests[17]. Additionally, it provides a comprehensive assessment of nutritional status by considering both nutritional and immune parameters[20]. Moreover, it has been shown to be an independent predictor of outcomes, even after adjusting for other known prognostic factors[20]. In a recent study, we retrospectively examined 232 patients who underwent radical cystectomy due to bladder cancer[22]. Our findings suggest that a preoperative high CONUT score may be an independent prognostic factor in patients undergoing radical cystectomy for bladder cancer[22,23].

In this study, we investigated the significance of using both the R.E.N.A.L. and CONUT scores in patients who underwent partial nephrectomy for kidney cancer. In addition, we analyzed factors that can contribute to these scoring systems.

MATERIALS AND METHODS

The study includes retrospective research of prospectively gathered data. All participants signed consent forms that were obtained. The ethical committee approved the study. Data from 115 patients who underwent partial nephrectomy (included clinical tumor size $\leq$ 7 cm) due to masses at a single experienced center between January 2015 and August 2023 were investigated. Twenty-seven patients were excluded from the study, including those with missing data. Age, gender,

Table 2. R.E.N.A.L. nephrometry scoring system

	R.E.N.A.L. Score		
	1 Point	2 Points	3 Points
(R)adius (maximal diameter in cm)	≤ 4	> 4 but <7	≥ 7
(E)xophytic/endophytic properties	≥ 50%	< 50%	Entirely endophytic
(N)earness of a tumor to the collecting system or sinus (mm)	≥ 7	> 4 but <7	≤ 4
(A)nterior/posterior (L)ocation relative to polar lines	No points were given. Mass assigned a descriptor of a, p, or x		
	Entirely above the upper or below the lower polar line	Lesion crosses the polar line	> 50% Of the mass across the polar line, or mass crosses the axial renal midline, or mass is entirely between the polar lines
	Low	Moderate	High
Total Score	4 – 6	7 – 9	10 - 12

Table 3. Patients' Demographic Data

Demographics	No. of patients/percent		*P* value
	Recurrence	Non - Recurrence	
Gender			
Male	12 (%19.4)	50 (%80.6)	0.216*
Female	2 (%7.7)	24 (%92.3)	
Age (mean) (Std. Deviation)	56,92 (± 6.83)	56,71 (± 10.47)	0.723**
Hypertension			0.003*
Yes	13 (%26)	37 (%74)	
No	1 (%2.6)	37 (%97.4)	
Diabetes Mellitus			0.033*
Yes	14 (%20.6)	54 (%79.4)	
No	0	20 (%100)	
Coronary Artery Disease	0,117*		
Yes	14 (%18.7)	61 (%81.3)	
No	0	13 (%100)	
Smoke			
Non - Smoker	4 (%11.4)	31 (%88.6)	0.363***
Smoker	10 (%21.3)	37 (%78.7)	
Ex - Smoker	0	6 (%100)	
Body Mass Index			
Normal	3 (%10)	27 (%90)	0.023***
Overweight	3 (%8.8)	31 (%92.2)	
Obesity	8 (%33.3)	16 (%66.7)	
Follow-up Month Median (range)			
	28.5 (0-91)	48 (9-60)	0.147**

* Fisher exact test
** Mann - Whitney *U* test
*** Chi - Square

body mass index (BMI), comorbidities (hypertension, diabetes mellitus), smoking status, tumor characteristics, CONUT, and R.E.N.A.L. scores were recorded. Exclusion criteria were previous surgery on the same kidney, any complication after partial nephrectomy, specimen pathology other than RCC, bilateral renal tumors, and tumors invading the same-side adrenal gland or perinephric region. Moreover, any preoperative drugs or conditions that may influence the variables of the CONUT score, infection, liver failure, or metabolic disease that can affect serum albumin levels were included as exclusion criteria.

All patients were regularly followed up at our outpatient clinic. Parameters related to survival were recorded by examining the national healthcare system database. The development of local recurrence during the follow-up period was determined as the endpoint of the study. Furthermore, all patients were followed up according to the European Guideline of Urology-Renal Cancer guideline of European Urology[9]. Recurrent inpatients were evaluated in our clinic council. The decision for recurrence was taken as a joint decision in the council involving experienced uroradiologist, urooncologist, and nuclear medicine specialists.

Statistical analysis

The Statistical Package for the Social Sciences (SPSS, Chicago, IL) version 16.0 was used. Significant p was $p < 0.05$.

Descriptive statistics were reported for categorical variables as counts and percentages and for continuous

Table 4. Tumor and Surgical Characteristics

Tumor and Surgical Characteristics	No. of patients/percent		*P* value
	Recurrence	Non - Recurrence	
Tumor Side			0.538*
Right	5 (%13.2)	33 (%86.8)	
Left	9 (%18)	41 (%82)	
Tumor T Stage			< 0.001**
T1	9 (%11)	73 (%89)	
T2	5 (%83.3)	1 (%16.7)	
Ischemia			0.509*
Ischemic	5 (%20)	20 (%80)	
Non - Ischemic	9 (%14.3)	54 (%85.7)	
Surgical Margine			< 0.001*
Negative	6 (%8.1)	68 (%91.9)	
Positive	8 (%57.1)	6 (%42.9)	
R.E.N.A.L Score			< 0.001*
Moderate	6 (%8.7)	63 (%91.3)	
High	8 (%42.1)	11 (%57.9)	
CONUT Group			< 0.001*
Normal	2 (%3.6)	53 (%96.4)	
Mild	1 (%6.3)	15 (%93.8)	
Moderate	8 (%61.5)	5 (%38.5)	
Severe	3 (%75)	1 (%25)	

* Chi – Square
** Fisher exact test

Table 5. The results of our multivariable analysis

	Univariate				Multivariable			
	p-value	HR	95% for EXP (B)		*p*-value	HR	95% for EXP (B)	
			Lower	Upper			Lower	Upper
Age	0.136	0.32	0.071	1.432				
Hypertension	0.095	0.176	0.023	1.053				
R.E.N.A.L. Score	0.001	6.765	2.268	20.176				
Surgical Margine	< 0.001	0.102	0.034	0.311	0.004	0.073	0.012	0.435
CONUT Score	< 0.001	3.017	1.822	4.997	0.001	3.221	1.617	6.418
T Stage	< 0.001	0.079	0.021	0.302				
Body Mass Index	0.035	2.44	1.067	5.579				

* Cox Regression

variables as means and standard deviations. The relationships between categorical variables were evaluated using the Chi-Square test, and in cases where the variable frequency was below 5, Fisher's Exact test was used. Independent two-group comparisons were made using the Mann-Whitney *U* test.

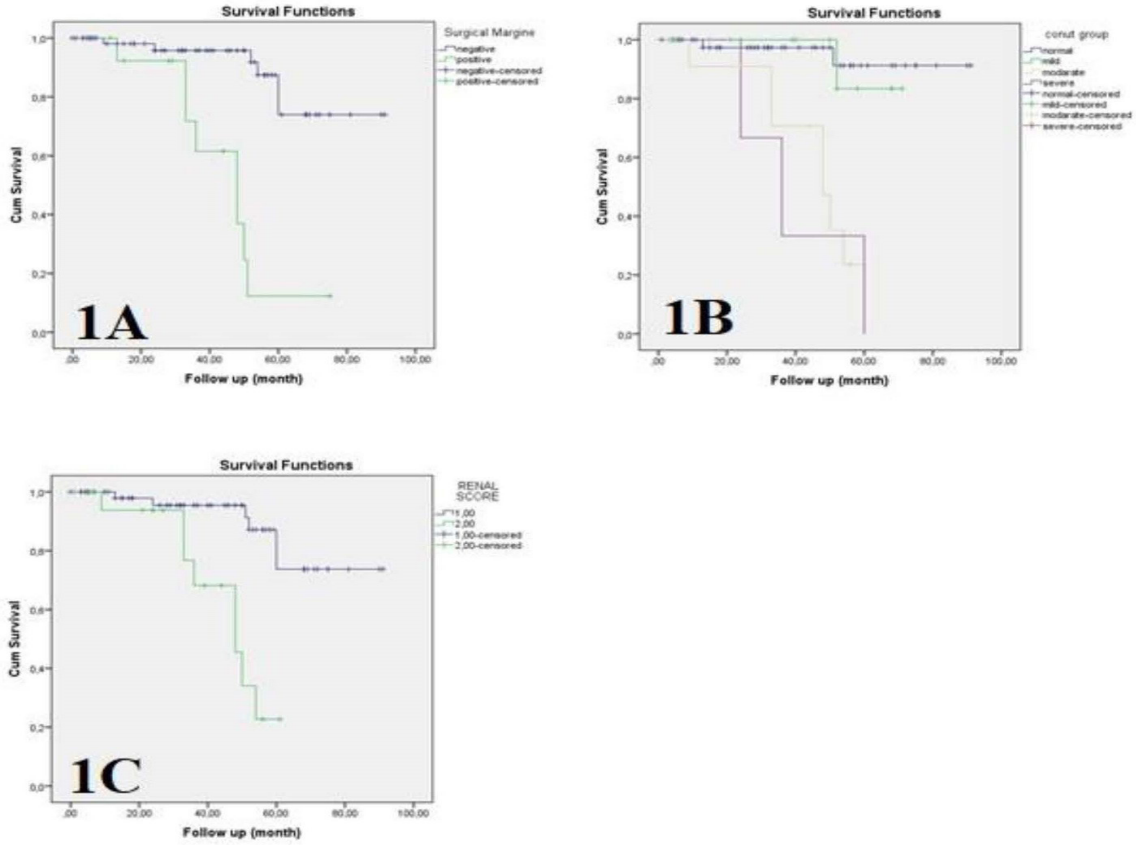
Univariate Cox Regression analysis was used to evaluate parameters for recurrence-free survival. The linearity for quantifiers, the hazard ratio, and the 95% confidence interval were calculated for each parameter, and variables with $p < 0.20$ were considered candidate risk factors and included in the multivariable model. Multivariable analysis was performed using the Multivariable Cox Regression analysis and variables. Kaplan-Meier curves were provided for variables that showed statistical significance in the multivariable analysis, and the Log-Rank test was used to compare these curves.

The CONUT score was calculated using values for serum albumin, total lymphocyte count, and total cholesterol concentration (**Table 1**).

RESULTS

In total, 88 patients were enrolled in the study. The mean age was 55.58 years. Of the patients, 26 (%29.54) were female and 62 (%70.45) were male. According to the analyses, gender did not have any statistical significance in terms of tumor recurrence. Fifty (%56.81) patients were diagnosed with hypertension, 68 (%77.27) with diabetes mellitus, and 75 (%85.22) with coronary artery disease. The presence of diabetes mellitus (p = 0.033) and hypertension (p = 0.003) was found to be statistically significant in terms of tumor recurrence. On the other hand, the presence of coronary artery disease was not found to be statistically significant in terms of tumor recurrence in our study (**Table 3**).

Thirty-five (%39.77) patients were non-smokers; additionally, 47 (%53.40) and 6 (%6.81) patients were



Figures 1A. Kaplan-Meier curves, Surgical Margin 1B. Conut Group, 1c. Renal Score.

either current smokers and/or ex-smokers. Although tumor recurrence appeared to be more frequent among smokers compared to non-smokers, it was not found to be statistically significant (**Table 3**).

Patients' BMI was calculated. Accordingly, 30 (%34.09) patients were normal weight, 34 (%38.63) were overweight, and 24 (%27.27) were obese. A high BMI was found to be statistically significant in terms of recurrence ($p < 0.05$) (**Table 3).**

The side of the tumor did not have any significance in terms of recurrence. On the other hand, a statistically significant positive correlation was observed between high tumor stage and recurrence. Among patients with T2 stage tumors, recurrence was observed in 5 out of 6 patients (83.3%). Furthermore, there were nine (%11) recurrences in patients with T1 ($p < 0.001$) (**Table 4**).

Ischemic procedures were performed on 25 patients (28.40%). When examining tumor recurrence in patients who underwent ischemic and non-ischemic surgical methods, there was no statistical significance.

Out of the 14 patients with positive surgical margins, tumor recurrence was observed in eight patients (57.1%). Six patients (8.1%) with no tumor on the surgical margin had a recurrence. Based on these data, surgical margin positivity was calculated to be statistically significant in terms of tumor recurrence ($p < 0.001$) (**Table 4**).

Tumor recurrence was higher in patients with high R.E.N.A.L. scores (42.1%) compared to those with moderate scores (8.7%), and this difference was statistically significant ($p < 0.001$) (**Table 4**).

CONUT Score was evaluated in four groups in our study. The rise in CONUT Score was statistically significant in terms of tumor recurrence ($p < 0.001$). The tumor characteristics and surgical method-related data of the patients are presented in **Table 4**.

In the multivariable analysis, surgical margin positivity ($p = 0.001$) and high CONUT Score (< 0.001) were statistically significant in terms of tumor recurrence. No recurrence was observed in patients with low R.E.N.A.L. scores. Therefore, the R.E.N.A.L. Score, which appeared significant in univariate analysis, did not show significance in multivariable analysis. The censored proportion was %59,1. The results of our multivariable analysis are presented in **Table 5**. Furthermore, Kaplan-Meier curves for the variables with statistically significant findings in the multivariable analysis are displayed in (**Figures 1)**.

DISCUSSION

In the present study, we evaluated the impact of R.E.N.A.L. and CONUT scores on recurrence after partial nephrectomy. The relationship between the CONUT score and the prognosis of urological cancers has been previously studied[22–26]. In cases of renal cell carcinoma, the CONUT score exhibited a significant association with overall survival, and its prognostic value surpassed that of other nutritional indicators, including the Prognostic Nutritional Index[27,28]. However, to the best of our knowledge, our study is the first to investigate the relationship between tumor recurrence after partial nephrectomy and a combination of these scores in the published literature. Our results supported the aim of the study as high CONUT Scores in patients with moderate (7-9) and high (10-12) R.E.N.A.L. Scores were statistically significant in terms of tumor recurrence ($p < 0.001$, OR: 2.898). Additionally, we found that patients with a high CONUT Score also had an increased rate of recurrence. This may suggest that these scores might be used to predict tumor recurrence, potentially leading to closer monitoring of patients or the consideration of more radical treatments.

In light of our results, clinicians should closely monitor and actively treat Type 2 diabetes mellitus (T2D) in RCC patients with the aim of improving their survival and reducing the recurrence rate. These findings pointed to the importance of T2D in determining the prognosis of RCC patients[29-31]. Additionally, our study identified that the presence of diabetes mellitus was statistically significantly associated with tumor recurrence in univariate analysis. These results indicate the necessity of closely monitoring these patients and considering these factors in treatment plans.

Potential risk factors for renal cell carcinoma are smoking, obesity, high body mass index, and hypertension [32–35]. In the patient groups, 50.2% of them were current or former smokers[36]. Published literature shows that the percentage of smoking can vary from 38% in chromophobe carcinoma (chRCC) patients to 61.9% in collecting duct/medullary carcinoma (kD/M) patients [36]. In our study, the relationship between smoking and tumor recurrence was observed but did not reach statistical significance.. However, considering the overall negative effects of smoking on health, our findings emphasize the importance of encouraging patients to give up smoking.

In our study, we found that a high BMI was associated with an increased risk of tumor recurrence. The research on this issue supported our results and indicated that a BMI might increase the risk of RCC (renal cell carcinoma)[37,38]. However, the relationship between high BMI and the risk of RCC recurrence is more complex. In RCC patients, a high BMI can potentially increase the risk of recurrence following surgery. Furthermore, high BMI is considered one of the risk factors for kidney cancer[38,39].

Other factors, such as the patient's overall health status, tumor stage, and characteristics, should also be considered. The risk of recurrence in partial nephrectomy patients should be assessed for multiple risk factors as our results showed statistical significance. Nevertheless, it should be noted that a high BMI is associated with tumour recurrence.

There are some limitations in the study. First, the study pattern is retrospective. The second, sample size is small. However, we used statistical tests and could get significant numbers. Thus, the results of the present study may be a pathfinder for future studies.

A strong positive relationship was observed between tumor stage and surgical margin positivity with recurrence. Tumors in stage T2 had a higher rate of recurrence. These findings highlighted the significant role of tumor stage and size in surgical treatment plans (40,41). In our study, patients with low R.E.N.A.L. scores did not experience recurrence. Therefore, patients with moderate and severe scores were evaluated in the study regarding tumor recurrence. To understand its value in tumor recurrence, the CONUT Score was calculated for patients with moderate and severe R.E.N.A.L. scores.

In summary, the CONUT score serves as a readily available and cost-effective biomarker that can complement existing or future stratification scores. Its prognostic value aids decision-making processes in clinical

settings. High R.E.N.A.L. and CONUT scores are important factors in RCC patients. Recurrence rates after surgery are strongly related to higher scores of these indexes. Combining these scores may enhance surgical success and enable surgeons to provide patients with more informed and tailored knowledge.

CONCLUSIONS

The recurrence rate after patient nephrectomy can be predicted by the unification of R.E.N.A.L. and CONUT scores. Higher scores might show higher recurrences. However, -the risk factors of RCC are very well known and may contribute to to these scores. In addition, comorbidities should be considered before surgical treatment. Clinicians should evaluate all these factors for successful treatment. More standardized multicentered studies are required for optimal decision-making regarding surgical treatment for partial nephrectomy.

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