

Role of R.E.N.A.L. Nephrometry Score in Laparoscopic Partial Nephrectomy

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Abstract

Background: Preoperative anatomical scoring system is conducive to comparison between treatment options and evaluation of postoperative outcomes in patients with small renal tumors. This study aimed to evaluate the clinical application efficacy of the R.E.N.A.L. nephrometry score (RNS) in predicting perioperative outcomes in patients with renal tumor who underwent laparoscopic partial nephrectomy (LPN).

Methods: The clinical data of 139 patients with renal tumors who underwent LPN between 2009 and 2015 were collected and analyzed. Patients were divided into three groups according to their RNS (low, moderate, and high). Clinical characteristics including perioperative variables, complications, and RNS were compared to evaluate the differences between the three groups. Multivariable logistic regression analysis was used to analyze the risk factors of postoperative complications.

Results: According to the RNS, there were 74, 50, and 15 patients in the low, moderate, and high RNS groups, respectively. There were significant differences in estimated blood loss (EBL; $\chi^2 = 7.285$, $P = 0.026$), warm ischemia time (WIT; $\chi^2 = 13.718$, $P = 0.001$), operation time (OT; $\chi^2 = 6.882$, $P = 0.032$), perioperative creatinine clearance change (PCCC; $\chi^2 = 6.206$, $P = 0.045$), and number of patients with complications (NPC; $P = 0.002$) among the three groups. The values for EBL, WIT, OT, PCCC, and NPC for patients in the high RNS group were higher than those for patients in the low RNS group. After adjustment for OT, WIT, and EBL, RNS was statistically significantly associated with the risk of postoperative complications in a multivariable logistic regression model (odds ratio = 1.541, 95% confidence interval: 1.059–2.242, $P = 0.024$).

Conclusions: The RNS is a valuable tool for evaluating the complexity of renal tumor anatomy. It can aid surgeons in preoperative decision-making concerning management therapy. Future multicenter, large sample size studies are warranted for evaluating its predicting performance of perioperative outcomes.

Key words: Laparoscopic Partial Nephrectomy; R.E.N.A.L. Nephrometry Score; Renal Cell Carcinoma

INTRODUCTION

Renal cell carcinoma (RCC) is the most common form of solid cancer of the kidney and comprises approximately 90% of all malignant renal tumors.^[1] Regrettably, most patients with RCC remain asymptomatic until the late stage of the disease. Nephron-sparing surgery (NSS) is recommended in patients with T1a tumors and is also favored in patients with T1b tumors when technically feasible.^[1] Open partial nephrectomy (PN) remains the established standard for removal of T1 tumors, but nowadays, laparoscopic PN (LPN) has gaining popularity over open PN owing to its advantages of less blood loss, reduced operation time (OT),

shorter hospital stay, and avoidance of morbidity related to flank incisions.^[2,3] However, LPN has a higher complication rate compared with open radical nephrectomy (RN) and it is also reported to be demanding and technically challenging for complex renal tumors.^[2,4]

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Preoperative anatomical scoring system is conducive to comparison between treatment options and evaluation of postoperative outcomes in patients with small renal tumors. The R.E.N.A.L. nephrometry score (RNS) proposed by Kutikov and Uzzo^[5] is based on the five most reproducible and pertinent features that characterize renal tumor critical anatomical attributes [Supplementary Table 1]. Previous studies have demonstrated its superiority in predicting perioperative outcomes.^[6-8]

We conducted a retrospective analysis of clinical data from 139 patients with renal tumors who underwent LPN in a tertiary center in Beijing, with the aim of sharing our experiences and evaluating the efficacy of RNS in predicting perioperative outcomes.

METHODS

Ethical approval

Clinical data were obtained from our database and approved by our Institutional Review Board and Medical Ethics Committee. The requirement for written informed consent from patients was waived because of the retrospective design of the study.

Patients and clinical data collection

From May 2010 to December 2015, 139 patients suspected of having RCC were admitted and treated in the Department of Urology, Beijing Chao-yang Hospital, Capital Medical University. Demographics and perioperative data were collected and analyzed [Table 1]. Patients with bilateral or multiple tumors or metastasis were excluded from this study.

Patients' data including age, sex, body mass index (BMI), comorbidities, symptoms, laterality of renal tumors, preoperative creatinine, and hemoglobin levels were collected and recorded. Intraoperative data included total OT, warm ischemia time (WIT), and estimated blood loss (EBL). Postoperative data included complications, length of hospital stay, postoperative creatinine and hemoglobin levels, tumor pathology and margins, follow-up period, and outcomes.

Surgical procedure

Following general anesthesia, patients were placed in lateral position, and three-port retroperitoneal LPN was performed. A retroperitoneal cavity was constructed by balloon dilation, followed by dissection of paranephric fat and Gerota's fascia. The renal vessels were dissected free, and the renal artery was then clamped with bulldog clamps to facilitate excision and suturing. Retrograde ureteral stent placement was performed under cystoscopy, if the renal tumor was located close to the renal pelvis. Methylene blue injection was performed to determine if suturing was sufficiently tight, to minimize the occurrence of postoperative urine leakage. LPN was performed in all patients by a single experienced senior urologist.

The RNS was used to evaluate tumor complexity by a retrospective review of imaging including computed tomography (CT) or magnetic resonance imaging (MRI;

Table 1: Demographic characteristics of patients who underwent laparoscopic partial nephrectomy

Characteristics	Results
Age (years)	52.4 ± 13.6
Gender	
Male	83/139 (59.7)
Female	56/139 (40.3)
BMI (kg/m ²)	25.3 ± 3.8
Comorbidity	
Arrhythmia	2 (1.4)
Adrenal pheochromocytoma	1 (0.7)
Breast disease	2 (1.4)
Benign prostatic hyperplasia	6 (4.3)
Cerebral disease	12 (8.6)
Coronary heart disease	8 (5.8)
Diabetes mellitus	21 (15.1)
Hypertension	49 (35.3)
Hysteromyoma	1 (0.7)
Peptic ulcer	3 (2.1)
Renal cyst	2 (1.4)
Urolithiasis	3 (2.1)
Symptoms	
Asymptomatic	94 (67.6)
Abdominal distension	3 (2.2)
Frequency	4 (2.9)
Fatigue	2 (1.4)
Fever	2 (1.4)
Mild backache	31 (22.3)
Hematuria	3 (2.2)
Laterality of renal neoplasm	
Left	65 (46.8)
Right	74 (53.2)

Data are presented as *n* (%) or mean ± SD. BMI: Body mass index; SD: Standard deviation.

both axial and coronal planes). All CT or MRI data were evaluated by a single senior radiologist. As described by Kutikov and Uzzo,^[5] the five components of RNS include: radius (maximal diameter), exophytic/endophytic properties, nearness of lesion to the collecting system or sinus, anterior (a) or posterior location of lesion, and location of the lesion relative to the polar lines. Suffix "h" was used to designate a hilar tumor. According to the RNS system, tumor complexity was defined as low, moderate, and high if the R.E.N.A.L. score was 4–6, 7–9, or 10–12, respectively. The Clavien–Dindo classification system^[9] was used to stratify the 30-day postoperative complications.

Statistical analysis

The continuous variables were described as the mean ± standard deviation (SD) and compared using one-way analysis of variance (ANOVA) for the normally distributed data. For skewed distributions, the data are presented as the median (interquartile range) and compared using the nonparametric Kruskal–Wallis and Mann–Whitney *U*-tests. The categorical variables were described as percentages and compared using the Pearson's Chi-squared and Fisher's exact tests. Multivariate logistic regression analysis was performed

to analyze potential determinants of the occurrence of postoperative complications. All analyses were performed using SPSS 22.0 statistical software package (SPSS Inc., Chicago, IL, USA). A two-tailed value of $P < 0.05$ was considered statistically significant.

RESULTS

Demographic characteristics of patients

According to the RNS system, among the 139 patients who underwent LPN, tumor complexity was low in 74 (53.2%) patients, moderate in 50 (36.0%) patients, and high in 15 (10.8%) patients. The demographic characteristics of the patients are shown in Table 2. The mean age of the patients

was 52.4 years and the mean BMI was 25.3 kg/m². Ninety-four patients were asymptomatic, and symptoms experienced by other patients included abdominal distension (three cases), fatigue (two cases), frequency (four cases), fever (two cases), backache (31 cases), and hematuria (three cases). Sixty-five patients had renal tumors on the left side while 74 patients had them on the right. Regarding comorbidities, 49 (35.3%) patients had hypertension and 21 (15.1%) patients had diabetes mellitus. Other comorbidities included cerebral disease (12 cases), coronary heart disease (eight cases), benign prostatic hyperplasia (six cases), peptic ulcer (three cases), urolithiasis (two cases), breast diseases (two cases), arrhythmia (two cases), adrenal pheochromocytoma (one case), and hysteromyoma (one case).

Table 2: Peri-operative data of patients who underwent laparoscopic partial nephrectomy

Items	Results
Tumor size (cm)	3.0 (2.5–4.1)
Operation time (min)	120 (105–150)
Estimated blood loss (ml)	100 (50–100)
Warm ischemia time (min)	20 (20–24)
Postoperative hospital stay (days)	7 (6–9)
Follow-up period (months)	24 (18–30)
Pathology results	
Clear cell carcinoma	109 (78.4)
Papillary cell carcinoma	1 (0.7)
Chromophobe cell carcinoma	5 (3.6)
Multilocular cystic renal cell carcinoma	3 (2.2)
Angiomyolipoma	19 (13.7)
Benign renal cyst	2 (1.4)
Complications	
Grade II	5 (45.5)
Blood transfusion	3 (27.3)
Total parenteral nutrition	2 (18.2)
Grade IIIb	4 (36.3)
Conversion to open surgery	4 (36.3)
Grade IVa	2 (18.2)
Renal dysfunction needing dialysis	2 (18.2)

Data are presented as median (Q1–Q3) or n (%).

Perioperative data

Perioperative data are shown in Tables 2 and 3. Regarding postoperative histopathology, 109 (78.4%) patients had clear cell carcinoma, 19 patients (13.7%) had angiomyolipoma, five patients (3.6%) had chromophobe cell carcinoma, three patients (2.2%) had multilocular cystic RCC, two patients (1.4%) had benign renal cysts, and one patient (0.7%) had papillary cell carcinoma. The mean follow-up period was 22.8 ± 9.5 months. The postoperative complications were categorized according to the Clavien–Dindo classification system. Eleven patients had complications, five of whom had Grade II complications. Grade IIIb complications occurred in four patients and Grade IVa complications occurred in two patients. Three patients underwent blood transfusion, and two received total parenteral nutrition. Four patients were converted to open surgery, and two had postoperative renal dysfunction that required dialysis. One patient had lung metastasis at 21 months postoperatively, while another had vertebrate metastasis at 9 months postoperatively.

The overall mean tumor diameter was 3.0 cm (range: 2.5–4.1 cm). There was no difference in patient age ($P = 0.527$), male/female ratio ($P = 0.880$), or BMI ($P = 0.430$) among the three groups of patients classified according to renal tumor complexity. The

Table 3: Perioperative variables of patients who underwent laparoscopic partial nephrectomy

Variables	Low ($n = 74$)	Moderate ($n = 50$)	High ($n = 15$)	Statistical value	P
Age (years)	51.2 \pm 13.3	53.8 \pm 14.8	53.8 \pm 9.9	0.644*	0.527
Male/female, n	44/30	31/19	8/7	0.364†	0.880
BMI (kg/m ²)	25.4 \pm 3.8	24.8 \pm 3.7	26.2 \pm 4.1	0.849*	0.430
EBL (ml)	100 (50–100)	100 (50–200)	100 (60–300)	7.285†	0.026‡
WIT (min)	20 (18–22)	22 (20–24)	28 (20–30)	13.718†	0.001§
OT (min)	120 (93.8–150.0)	120 (118.8–157.7)	165 (120.0–210.0)	6.882†	0.032
PHS (days)	7 (5.0–8.3)	7 (6–9)	8 (5–9)	1.654†	0.437
PCCC (ml/min)	11.5 (1–23)	13.5 (1.8–29.5)	31 (10–51)	6.206†	0.045¶
NPC, n (%)	5 (6.8)	1 (2.0)	5 (33.3)	–	0.002**
RNS	4.9 \pm 0.7	7.6 \pm 0.6	10.7 \pm 0.7	114.106†	0.000††

Data are presented as mean \pm SD, median (Q1–Q3), or n (%). *: F values; †: χ^2 values; ‡Low < moderate ($P = 0.047$), low < high ($P = 0.023$); §Low < high ($P = 0.023$), low < moderate ($P = 0.005$); ||Low < high ($P = 0.034$); ¶Low < high ($P = 0.013$); **Low < high ($P = 0.011$), moderate < high ($P = 0.002$); ††Low < moderate ($P = 0.000$), low < high ($P = 0.000$), and moderate < high ($P = 0.005$). –: Not applicable; EBL: Estimated blood loss; WIT: Warm ischemia time; OT: Operative time; PHS: Postoperative hospital stay; PCCC: Perioperative creatine clearance change; NPC: Number of patients with complications; RNS: R.E.N.A.L. nephrometry score; SD: Standard deviation; BMI: Body mass index.

Table 4: Multivariable analysis of postoperative complications of laparoscopic partial nephrectomy

Variables	β	Wald	OR	95% CI	P
OT	0.009	1.900	1.009	0.996–1.023	0.168
WIT	0.034	0.351	1.034	0.925–1.156	0.553
EBL	0.002	0.517	1.002	0.996–1.009	0.472
MD	-0.478	2.073	0.620	0.323–1.189	0.150
RNS	0.432	5.108	1.541	1.059–2.242	0.024

OT: Operation time; WIT: Warm ischemia time; EBL: Estimated blood loss; MD: Maximal diameter; RNS: R.E.N.A.L. nephrometry score; OR: Odds ratio; CI: Confidence interval.

overall mean OT was 120 min (range: 105–150 min), the overall mean postoperative hospital stay (PHS) was 7 days (range: 6–9 days), and the overall mean EBL was 100 ml (range: 50–100 ml). There was no significant difference in PHS ($P = 0.437$) among the three groups. However, there were significant differences in EBL ($P = 0.026$), WIT ($P = 0.001$), OT ($P = 0.032$), perioperative creatinine clearance change (PCCC) ($P = 0.045$), and the number of patients with complications (NPC) ($P = 0.002$) among the three groups. The values of EBL, WIT, OT, PCCC, and NPC for patients in the high tumor complexity group were greater than those for patients in the low complexity group [Table 4]. Six patients underwent off-clamp LNP (zero-ischemia).

Regarding postoperative complications, multivariable logistic regression analysis indicated that the RNS was statistically significantly associated with the risk of occurrence of postoperative complications ($P = 0.024$) [Table 4].

DISCUSSION

Thanks to the increasing utility of various kinds of abdominal imaging modalities, the detection of small renal masses has increased in the recent years. In the past decade, there has been a shift from RN to NSS. At present, NSS has become the golden standard for the treatment of small renal tumors.^[10] Compared with RN, NSS provides long-term benefits for cancer control and preservation of renal function. Studies in the recent years have confirmed lower blood loss, postoperative pain, and shorter convalescence period alongside small incisions as the primary advantages of LPN.^[11] Additionally, more recent therapeutic advancement of technologies such as robotic-assisted PN (RAPN) and thermal ablation have expanded the treatment options. However, treatment recommendations vary and depend largely on the anatomical characteristics of tumors and the experience of urologists in making optimal decisions for treatment.

In the recent years, apart from the RNS, several other nephrometry scoring systems have been proposed to predict perioperative outcomes. The centrality index scoring (C-index) uses the Pythagorean theorem to calculate the distance from the tumor center to the kidney center and then this distance is divided by the tumor radius to obtain the C-index.^[12] It was reported to serve as a clinically useful measure, allow improved clinical and radiological

assessment of kidney tumors, and may be more suitable than the RNS in predicting postoperative renal function.^[13] The Preoperative Aspects and Dimensions Used for an Anatomical (PADUA) classification proposed by Ficarra *et al.* evaluates anatomical features such as anterior or posterior face, longitudinal, and rim tumor location, tumor relationships with renal sinus or urinary collecting system, and percentage of tumor deepening into the kidney. It is reported to be a simple scoring system that can be used to predict perioperative complications.^[14] Ricciardulli *et al.* suggested that PADUA score can serve as a predictor of WIT during LPN.^[15] The Zonal NePhRO Scoring (ZNS) system based on four anatomical components (nearness to collecting system, physical location of the tumor in the kidney, radius of the tumor, and organization of the tumor) is a simple tool that accurately predicts surgical complexity of renal lesions.^[16] Kriegmair *et al.* showed that the ZNS can predict perioperative complications in patients undergoing open PN.^[17] As to RNS system, Borgmann *et al.* concluded that the RNS correlates best with tumor margin, ischemia, and the occurrence of complications and quantitative perioperative outcomes of NSS.^[6] Schiavina *et al.* showed that both the PADUA and RNS systems were significantly correlated with predicting prolonged WIT and high-grade postoperative complications after RAPN,^[18] while Osawa *et al.* showed that renal mass biopsy outperforms the RNS in discriminating between malignant versus benign tumors and low-risk versus high-risk tumors.^[19] The RNS was also reported to be a reproducible standardized classification system that quantitates the salient anatomy of renal tumors.^[5] A prospective study performed by Matos *et al.*, which included 71 patients, showed that the RNS was a good method in predicting surgical access route and type of nephrectomy, and the RNS was also associated with OT and WIT, but with weak accuracy.^[20] Kriegmair *et al.* conducted a systemic comparison of the aforementioned nephrometry scoring systems and concluded that all scoring systems represent objective and reproducible measurement tools for renal tumor complexity, and that the RENAL, PADUA, and NePhRO scores are comparable and seem to be more superior to C-index.^[21] Therefore, preoperative standardized analysis of renal tumor characteristics is essential for the determination of the method of treatment and for the comparison of the effectiveness of different treatments.

We retrospectively analyzed 139 patients with renal tumors treated by LPN at our solitary center. According to the RNS, 74 patients had low-complex tumors, 50 patients had moderate complex tumors, and 15 patients had high-complex tumors. Statistical analyses revealed that there were significant differences in OT, EBL, and WIT between the three groups. The OT, EBL, and WIT increased with increasing tumor complexity. The OT, EBL, and WIT in the high-complex group were significantly higher than those in the low-complex group. These data suggest that renal tumors with high complexity required increased cross-clamp time and are associated with more blood loss compared with those with low complexity, which may explain the PCCC between the three groups.

There were 11 cases with perioperative complications in our study. Four patients converted to open surgery, of which three patients (75%) are with high-complex tumors. There was a significant difference in the morbidity of complications between the three groups. The morbidity of complications in the high-complex group was higher than that in the low- or moderate-complex group. Multivariable regression analysis revealed that RNS is a risk factor that predicts the occurrence of perioperative complications. Previous studies have obtained similar results and demonstrated that the RNS is a useful tool in predicting the risk of complications in patients undergoing PN and laparoscopic renal cryoablation.^[22-25] Moreover, in patients who underwent robot-assisted PN, Schiavina *et al.* reported that RNS was significantly associated with predicting prolonged WIT and high-grade postoperative complications.^[18]

The mean follow-up period in our study was 22.8 ± 9.5 months (range: 1–44 months), and we identified two cases of postoperative metastasis. Mouracade *et al.* showed that high R.E.N.A.L. score increases the risk of disease recurrence after PN and R.E.N.A.L. score can predict local recurrence.^[26] Nagahara *et al.* reported that the RNS was an independent predictor of postoperative recurrence in patients with nonsmall localized RCC treated by PN.^[7] However, Mufarrij *et al.* showed that nephrometry-graded tumor complexity was not related to the surgical outcomes of patients who underwent RAPN, suggesting that the nephrometry system may be not suitable for predicting surgical outcomes,^[27] while Wang *et al.* modified the quantization parameters of the RNS system and demonstrated that the modified RNS system has a good effect in evaluating the operation difficulty of retroperitoneal PN.^[28]

The limitation of our study lies in the relatively small sample size and the retrospective nonrandomized single-center design, as these can result in selection bias and do not allow for the collection and analysis of all clinical data from all patients. Another limitation was that our results were based on the experience of a single surgeon. The results may therefore have been affected by the surgeon's learning curve of LPN. In addition, the mean follow-up period was 22.8 ± 9.5 months. This relatively short follow-up period may not exactly reflect the postoperative conditions of the patients. Future randomized, large sample size, and multicenter studies with longer follow-up periods are required to further validate our results.

In conclusion, we investigated the efficacy of clinical application of the RNS system for the prediction of peri-operative outcomes. The RNS is a standardized and feasible classification system for the evaluation of renal tumors. RNS can be used to evaluate tumor complexity and can aid surgeons in preoperative decision-making concerning management therapy.

Supplementary information is linked to the online version of the paper on the Chinese Medical Journal website.

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Conflicts of interest

There are no conflicts of interest.

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Supplementary Table 1: Description of the RNS system

Items	1 point	2 points	3 points
(R) Radius (maximal diameter in cm)	≤ 4	>4 but <7	≥ 7
(E) Exophytic/endophytic properties	$\geq 50\%$	$<50\%$	Entirely endophytic
(N) Nearness of the tumor to the collecting system or sinus (mm)	>7	>4 but <7	<4
(A) Anterior/posterior	Mass assigned a descriptor of a, p, or x. No points given		
(L) Location relative to the polar lines	Entirely above the upper or below the lower polar line	Lesion crosses polar lines	$>50\%$ of mass is across polar line (a) or mass crosses the axial renal midline (b) or mass is entirely between the polar lines

RNS: R.E.N.A.L. nephrometry score.