Can the R.E.N.A.L Nephrometry Score Preoperatively Predict Postoperative Clinical Outcomes in Patients Undergoing Open and Laparoscopic Partial Nephrectomy?

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Key Words

Partial nephrectomy • RENAL score

Abstract

Aim: We evaluate whether the preoperative R.E.N.A.L Nephrometry Score (RNS) can predict the postoperative outcomes in patients undergoing either an open or laparoscopic partial nephrectomy. **Patients and Methods:** We retrospectively calculated the RNS of 128 patients who underwent either an open partial nephrectomy (OPN) (n = 38) or laparoscopic partial nephrectomy (LPN) (n = 90) between 2003 and 2011. Patients were categorized into low, moderate or high complexity groups based on RNSs. Intra-operative warm ischemic time (WIT), peri-operative surgical outcomes using the Clavien-Dindo classification, postoperative histology, positive surgical margin rates were correlated to the RNS. **Results:** The RNS was associated with the length of the WIT in OPN (low vs. moderate vs. high: 11.4 vs. 13.1 vs. 23.4 minutes, p = 0.025) and blood loss in LPN (low vs. moderate 319 vs. 498 ml, p = 0.009). The positive surgical margins were greater in high versus moderate RNS lesions (40 vs. 7.4%, p = 0.045). No differences were seen in complications, hospital stay or transfusion rates. The RNS was significantly higher in OPN versus LPN (7.45 vs. 6.2, p = 0.0002). **Conclusion:** An Increasing RNS was associated with increased WIT in OPN and blood loss in LPN, supporting RNS relationship to tumor complexity. A higher RNS in OPN indicate it may corroborate procedure choice. RNS should allow comparisons

between treatment modalities for similar complexity lesions and with further research could aid stratification of individual risk preoperatively.

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Introduction

The incidence of renal cell carcinoma is increasing worldwide with a rise of more than 2% annually [1–4]. This may be due to an increase in routine radiological imaging for investigation of abdominal pain, resulting in > 60% of tumors being detected incidentally as small renal masses (T1a < 4 cm) on CT scan [5–7].

The recommended management of T1a tumors has evolved significantly over recent decades with partial nephrectomy being offered to suitable patients with small renal tumors, as per European Association of Urology and the National Institute for Health and Clinical Excellence guidelines [8, 9]. In current clinical practice the absolute indication of a partial nephrectomy include solitary kidney and bilateral synchronous tumors; relative indications include unilateral mass with preoperative risk for future renal impairment (e.g. Von Hippel-Lindau disease) and tumors less than 4 cm. A laparoscopic partial nephrectomy (LPN) has a higher complication rate

Table 1. The RNS categorization (2009) [17]

Anatomical features	Score		
	1 point	2 points	3 points
Radius (maximal diameter in cm)	≤4	> 4 but < 7	≥7
Exophytic properties	≤50%	> 50%	entirely endophytic
Nearness of tumor to collecting system or sinus (mm)	≥ 7	> 4, < 7	≤4
Anterior/posterior			
Location relative to the polar line	no points; descriptor a, p or x entirely above the upper or below the lower polar line	lesion crosses polar line	> 50% mass is across polar line (a) or crosses axial renal midline (b) or entirely between polar lines (c)

Sum of 4–6 =Low complexity; 7–9 = moderate complexity; 10 high complexity.

compared to open radical nephrectomy, varying between 5.5 and 38% [10]. This is in part attributable to risk of urinary fistula (4.4%) and technical difficulty [11]. Current literature indicated that a LPN remains underused worldwide [12, 13], but specialist centers are progressing quickly towards minimally invasive (laparoscopic and robotic) partial nephrectomy [14].

The current advantages of a LPN over open partial nephrectomy (OPN) include reduced blood loss, shorter total operation time, shorter hospital stay, reduced analgesic requirement and avoidance of morbidity related to large flank incisions [5, 15]. The oncological outcomes of both an OPN and LPN are currently comparable [16]. In certain situations the disadvantages of a LPN include a restricted exposure and intricate suturing, resulting in more difficult hemostasis and urinary system closure, longer warm ischemia time (WIT) all resulting in a higher per-operative complication rate [5]. Improvements in LPN have encouraged operations on more challenging tumors [5, 15].

In current literature there are no randomized controlled trials comparing active surveillance, LPN, OPN, radio frequency ablation or cryotherapy in the management of small renal masses. Inconsistencies in preoperative anatomical reporting and complications to date have hindered comparative studies and moreover the decision-making process for operative approach not clearly defined. It is now thought that a through preoperative anatomical scoring system will facilitate comparisons between treatment options for patients with

small renal masses and strengthen the rationale behind procedure choice and predict postoperative outcome. The R.E.N.A.L Nephrometry Score (RNS) is based on 5 reproducible and salient features related to diagnosed tumor preoperative [17] (table 1). However, results have been variable with respect to RNS as a predictor of outcomes. We evaluate whether the preoperative RNS can aid urologist in recommending either an OPN or LPN in patients being considered for partial nephrectomy.

Patients and Methods

From 2003 to 2011, 195 patients underwent OPN or LPN at our center. CTs were retrievable in 128 patients (90 LPN, 38 LPN). The remainder of the 67 patients were excluded as no preoperative imaging could be archived for the purpose of this study. On obtaining patient records and preoperative imaging the preoperative patient data was recorded, including patient age, previous renal surgery, creatinine and presenting complaint. Intra-operative data included WIT, total operation time and blood loss. Postoperative outcomes evaluated were transfusion rates, complications, length of hospital stay, surgical margins, histology, postoperative creatinine and recurrence. All patients underwent a transperitoneal LPN and OPN in our cohort. A total of 11 patients had single kidney (5 OPN and 6 LPN).

Preoperative CT was evaluated by a single radiologist. Total RNS sum was calculated and complexity category assigned: 4–6 low complexity; 7–9 moderate complexity; 10 high complexity. Complications were categorised into main urological complications and by Clavien-Dindo classification.

Statistical analysis compared low, moderate and high complexity groups using Kruskal Wallis and Mann Whitney-U non-parametric tests for numerical variables. Chi-squared and

Fisher's exact test were used for frequency distributions. RNS as a predictor of outcomes was then evaluated for open and laparoscopic groups separately. Where outcomes correlated to RNS group, linear regression was performed based on numerical value of RNS. Laparoscopic and open RNS were compared using 2 tailed T-test. Statistical analysis was performed using Excel 2003 with Analyse-It software.

Results

Patients were categorized into complexity groups: 55 (43%) low complexity (RNS 5–6); 68 (53.1%) moderate complexity (RNS 7–9); 5 (3.9%) high complexity (RNS 10). No LPNs were performed on high complexity lesions. The breakdown of open, laparoscopic and RNS category is shown in figure 1. The mean follow-up is 52 months (range 6–110 months) for the current cohort of all patients.

Tumor diameter and Individual RNS components are shown in table 2, represented by 'mean $\pm$ 95% CI (confidence interval) (median)'. Each component significantly differed between groups, indicating all contributed to tumor stratification. Although mean diameter differed between groups, median R score was 1 for all groups, as anticipated given partial nephrectomies are generally performed on small tumors.

RNS and Partial Nephrectomy Combined Outcomes

Outcomes of all partial nephrectomy are summarised in table 3 displayed as 'mean $\pm$ standard error, (median)'. P values < 0.05 were considered significant.

RNS category was not significantly associated with operation time, blood loss, WIT, hospital stay, transfusion rates, or complications in the combined LPN/OPN group. Creatinine change was associated with increasing RNS group, but this was not sustained on high-low or high-moderate comparison. Blood loss was significantly higher in the moderate compared to low complexity group (493.7 vs. 315.6 ml, $p = 0.03$). Positive margins were significantly higher in the high RNS than moderate RNS group (40 vs. 7.4%, $p = 0.045$). Operation time trend was reversed: shorter in high complexity lesions, though must be interpreted with caution given low numbers in the high RNS category.

Complications were categorised further into urological complications and Clavien-Dindo classification as shown in table 4. Overall complications occurred in 25.8% of cases – 17.4% major and 9.4% minor.

Mean RNS did not differ between cases with complications and those without (6.45 vs. 6.6, $p = 0.58$). Mean

RNS for those with major complications did not differ to RNS for minor/no complications (6.76 vs. 6.53, $p = 0.65$). Urine leak occurred in 5 patients (3.9%), 3 of which were LPNs and 2 OPNs. Completion nephrectomy was necessary in 1 patient, hemicolectomy/splenectomy in another, 2 required stenting/draining and 1 managed conservatively. Mean RNS ($\pm$ 95% CI; median) of those with leak versus no leak was 7.4 ($\pm$ 2.9; 8) versus 6.54 ($\pm$ 0.29; 7) which did not reach significance.

RNS Category and Tumor Pathology

Distribution of pathology can be viewed in figure 2. Histology was missing for 1 high and 1 moderate complexity lesion. Benign tumors occurred in 10.9% low complexity RNS, 3.4% moderate and 25% high complexity lesions ($p = 0.12$). High grade cancer appeared to increase with RNS, but this was insignificant: 14.6 vs. 26.3 vs. 33% low vs. moderate vs. high complexity lesions ($p = 0.3$).

LPN Outcomes

LPN outcomes analysed separately are summarised in table 5. In this subgroup no high complexity lesions were operated on. A significant difference was demonstrated between blood loss, but not other outcomes.

OPN Results

Results are summarised in table 6. In this subgroup WIT differed significantly: 11.4 vs. 13.1 vs. 23.4 minutes ($p = 0.025$). This difference was sustained between low-high and moderate-high groups, but not between low-moderate groups. On linear regression RNS was significantly correlated to WIT ($p < 0.001$). No other variables differed significantly between the groups.

RNS and Procedure Choice

Distribution of complexity categories was significantly different between LPN and OPN ($p = 0.0002$): low complexity tumors accounted for 23.7% OPN vs. 51% LPN; moderate tumors 63.2% OPN vs. 49% LPN; high complexity tumours 13.2% OPNs vs. 0% LPNs. Mean RNS was significantly lower in LPN than OPN RNS (6.2 ± 0.3 vs. 7.45 ± 0.6 , $p = 0.0002$).

Discussion

Early comparative studies between treatment modalities used anatomical parameters such as tumor size and polar location. The RNS is intended to record salient an-

Fig. 1. Flow diagram of procedure breakdown and complexity categories.

Table 2. Individual RNS scored variables

	Low (n = 55)	Moderate (n = 68)	High (n = 5)	p
Diameter (mm)	26.8 ± 1.8 (27)	33 ± 3.51 (30)	38.6 ± 28.9 (32)	0.008
RNS sum	5.01 ± 0.22 (5)	7.6 ± 0.19 (7)	10 ± 0 (10)	< 0.001
Radius score	1.05 ± 0.06 (1)	1.25 ± 0.12 (1)	1.4 ± 1.11 (1)	0.02
Exophytic score	1.27 ± 0.12 (1)	1.79 ± 0.14 (2)	2.6 ± 1.11 (3)	< 0.001
Nearness score	1.4 ± 0.18 (1)	2.68 ± 0.15 (3)	3 ± 0 (3)	< 0.001
Location score	1.31 ± 0.16 (1)	1.94 ± 0.27 (2)	3 ± 0 (3)	< 0.001

Single number in parentheses of the boxes is the median value.

Table 3. Individual RNS scored variables

	Low RNS (n = 55)	Moderate RNS (n = 68)	High RNS (n = 5)	p	Low-mod- erate p	Moderate-high p	Low- high p
Operation time (minute)	147.2 ± 7.1 (147.5)	144.7 ± 5.3 (135)	105 ± 10 (100)	0.08	0.88	0.03	0.03
Blood loss (ml)	315.6 ± 52.1 (200)	493.7 ± 63 (350)	246 ± 90 (180)	0.07	0.03	0.3	0.8
WIT (minute)	19.2 ± 1.1 (18)	20.4 ± 1.3 (19)	23.4 ± 4.2 (19)	0.61	0.56	0.48	0.38
Hospital stay (day)	6.8 ± 0.56 (6)	8.3 ± 0.9 (6)	8 ± 1.8 (7)	0.51	0.41	0.5	0.34
Transfusion rate (%)	5.45	8.88	0	0.63	–	–	–
Complications (%)	29	22	20	0.65	–	–	–
Positive margins (%)	10.9	7.4	40	0.16	0.54	0.045	0.085

Single number in parentheses of the boxes is the median value.

Table 4. Complications by RNS category

	Low	Moderate	High	p
All complications	29%	22%	20%	0.65
Major complications	20%	19.3%	20%	0.97
Urine leak	3.6%	2.9%	20%	0.16
Pseudoaneurysm	5.45%	7.35%	0%	0.76

Fig. 2. Individual RNS scored variables.**Table 5.** LPN outcomes

	Low RNS (n = 46)	Moderate RNS (n = 44)	p
Operation time (minute)	153 ± 7.72 (150)	151 ± 5.56 (145)	0.96
Blood loss (ml)	319.22 ± 58.45 (200)	498.14 ± 62.3 (400)	0.009
WIT (minute)	20.7 ± 1.09 (19)	23.6 ± 1.55 (23.5)	0.1
Hospital stay (day)	6.71 ± 0.64 (6)	6.48 ± 0.49 (5.5)	0.99
Transfusion rate (%)	4.35	6.82	0.62
All complications (%)	24.3	18.9	0.86
Urine leak (%)	4.3	2.3	1
Pseudoaneurysm (%)	8.7	4.5	0.72
Creatinine change (%)	-3 ± 0.5	13 ± 11	0.1
Positive margins (%)	8.76	4.5	0.67

Single number in parentheses of the boxes is the median value.

Table 6. OPN outcomes

	Low RNS (n = 55)	Moderate RNS (n = 68)	High RNS (n = 5)	p	Low-mod- erate p	Moderate-high p	Low- high p
Operation time (min)	112.5 ± 12.5 (100)	130 ± 11.3 (120)	105 ± 10 (100)	0.51	0.36	0.36	0.94
Blood loss (ml)	292 ± 101 (150)	456 ± 158 (180)	246 ± 90 (180)	0.96	0.85	0.91	0.87
WIT (minute)	11.4 ± 2.3 (11.5)	13.1 ± 1.2 (14)	23.4 ± 4.2 (19)	0.025	0.27	0.023	0.019
Hospital stay (day)	7.25 ± 0.84 (7)	11.87 ± 2.3 (8)	8 ± 1.78 (7)	0.76	0.46	0.78	0.93
Transfusion rate	11%	12.5%	0%	0.71	–	–	–
All complications	33%	33%	20%	0.83	–	–	–
Urine leak	0%	4.3%	20%	0.25	–	–	–
Pseudoaneurysm	0%	12.5%	0%	0.39	–	–	–
Creatinine change (%)	12.3 ± 19.2 (0)	26.6 ± 12.6 (10)	-1.6 ± 14 (-4)	0.29	0.26	0.25	0.92
Positive margins (%)	22.2	12.5	40	0.33	0.6	0.13	0.54

Single number in parentheses of the boxes is the median value.

atomical features associated with resection difficulty to produce a score which corresponds to tumor complexity. Having been validated as reproducible [18], several studies have emerged demonstrating its variable prediction of complications and outcomes [19–22].

In our study RNS association to outcomes was modest. RNS was significantly associated with blood loss in LPN (and pairwise low-moderate in combined partial nephrectomy), WIT in OPN and positive margin rates. Positive margins were similar between low and moderate groups but significantly different between moderate-high and nearing significance low-high suggesting scores 10 are most predictive and differentiation between low-moderate less important. Similarly, within the OPN group, WIT was not statistically significant between the low-moderate groups suggesting high complexity scores are more predictive for longer WIT.

Widely varying complication rates of partial nephrectomy have been documented between 5.5 and 38% [10]. Risk factors for complications include prolonged WIT, higher blood loss, tumor location and solitary kidneys [11, 19]. Urological complications include urinary leak, perinephric hemorrhage and renal impairment. Complications arose in 25.8% of our cases, with urine leak rates 3.9%, comparable to contemporary series [10]. No differences were seen between complexity groups or between RNS and major complications, contrary to that previously described by the RNS founders [20], although not proven universally [21].

The Fox Chase Cancer Center (founders of RNS) showed significant differences in major complication

rates (11.5%): 6.4 vs. 11.1 vs. 21.9% (low vs. moderate vs. high, $p = 0.009$) in 390 robotic (55.4%) and open (44.6%) partial nephrectomy [20]. Of note, this study had a larger proportion of high (16.4%) and moderate (55.6%) lesions. Genitourinary complications including urinary leak (1.8% low, 10.1% moderate, 28% high; overall 10.8%) differed significantly ($p < 0.0001$), but these appear rather high leak rates. Estimated blood loss and WIT differed significantly between the high-low/moderate groups. On multivariable logistic regression, operative time and high tumor complexity (RNS 10–12) were associated with major complication, odds ratio of the latter 5.4, CI: 1.2–24.2.

External validation has not been uniform. Positive results were reported by Bruner et al. [22] in a study of urine leak in 1,075 partial nephrectomies and 2.9% developed clinically significant urine leak, with a 35% increased odds for each unit increase in RNS. Of the individual components, location was found to have a reverse association i.e. polar location was associated with higher leak rates, raising the possibility this RNS component may not accurately assess tumor complexity. Those with urine leak also had longer hospital stay (6.8 vs. 4.4 days, $p = 0.019$) and higher complication rates compared to case-matched controls: haemorrhage (9.7 vs. 1.6%, $p = 0.05$); any complication (48.4 vs. 22%, $p < 0.001$). The authors did not stratify results into low/moderate/high RNS categories and so is unclear whether these categories are usefully assigned. Hew et al. [23] also described RNS correlation with complications (RNS > 9, odds ratio 4.21, $p = 0.02$) and was strongly predictive of WIT

($p < 0.001$). However, only $RNS > 9$ was a significant predictor, indicating little benefit of stratifying low and intermediate groups.

Hayn et al. [21] reported less convincing results in 159 consecutive LPNs. As in our study, only small numbers were high complexity lesions (30% low, 65% moderate, 5% high). Complication rates did not differ. Blood loss increased with RNS complexity category ($p < 0.034$), but no difference reported in transfusion rates. In agreement with the Fox Chaser study, longer WIT was seen in the higher complexity groups (16 vs. 23 vs. 31 minutes, $p < 0.001$), but this did not equate to any difference in GFR. Similarly, Okhunov et al. [18] associated RNS with WIT and change in creatinine level in 101 LPNs, but again no significant difference existed between complications, operative time or blood loss. Murfarrij et al. [24] found no differences in blood loss, operation time, hospital stay, GFR or complications in 92 robotic partial nephrectomies. However, the proportion of low complexity tumors was relatively high.

When comparing studies supportive of RNS as a predictor of complications to those showing no association, there are no definitive influencing factors. Patient cohort ages appear similar, varying distribution of low/moderate/high lesions appear in both situations and operative approach variable. Interestingly, the studies with only robotic or laparoscopic cases did not support RNS as a predictor of complications, although these had low percentage of high RNS (about 5 vs. 16.4%, Simham et al. [20]).

Despite disparity in correlation to other outcomes, RNS association with WIT, a key step in the operation, would support its relationship to tumor complexity. High RNS appears more predictive than moderate/low RNS, indicating studies may not show significance dependent on caseload complexity. This, however, raises the issue of cut-offs for the moderate and low groups and their role where the majority of subjects fall into these categories.

Positive margins in the present study appear high at 9.4% (18.4% open, 6.67%) compared to other studies' about 0–5% [5, 15]. However, there was only 1 definite recurrence within the positive margin group who had a history of left radical nephrectomy and radiotherapy for cerebral metastases, hence a high-risk patient. With such discrepancy in positive margin: recurrence rates, our figures are possibly due to classification and local pathological analysis.

Several papers have assessed RNS relationship to procedure choice, comparing radical to partial nephrectomy and also laparoscopic approaches [25–27]. As expected

in our study, OPN had higher RNS sum than LPN, in keeping with RNS use in stratifying tumour complexity.

Limitations exist within the present study. The time interval of 8 years may have created inaccuracies with learning curve dynamics and change in techniques. Three surgeons performed procedures, with possibly differing complication rates – operations were not analysed separately as greater numbers would have been required to provide adequate power. Finally, grouping LPN and OPN together may have skewed results and hence both were evaluated separately – unfortunately this led to small sample sizes. Previous studies have shown most positive results in high RNS category – given we had only 5 high complexity masses, significant differences may have been missed. In our study, the individual component of the RNS has not been correlated to evaluate outcomes in neither the OPN nor LPN group.

Conclusions

RNS offers a reproducible standardising anatomical reporting system. Although RNS correlation to operative outcomes is variable, the association with WIT supports its relationship to tumor complexity. RNS should allow for plausible comparisons between treatment modalities, particularly as more challenging tumours are operated on by laparoscopic and robotic partial nephrectomy. Further research into RNS as a predictive tool and as part of useable nomograms is required. Ideally this anatomical scoring tool could aid stratification of individual risk preoperatively, corroborate procedure choice and allow comparisons between treatment modalities for similar complexity lesions.

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