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# External validation of the RENAL nephrometry score in renal tumours treated by partial nephrectomy

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## What's known on the subject? and What does the study add?

- Using a standardized classification for renal tumours is a major step towards an objective comparison of the indications and expected outcomes of partial nephrectomy (PN).
- Several scores have been described, including the RENAL nephrectomy score (RNS), to evaluate the anatomical features of a renal tumour and predict the surgical challenges with particular regard to PN. Previous studies show discrepancies with regard to the effectiveness of using the RNS to predict postoperative outcomes. Although we showed that conversion to radical nephrectomy was predicted by the RNS, the occurrence of complications was more difficult to predict.

## Objective

- To evaluate the RENAL nephrometry score (RNS) as a predictor of the perioperative outcomes of a partial nephrectomy.

## Patients and Methods

- A retrospective review of 177 consecutive patients who were candidates for an open partial nephrectomy (OPN,  $n = 159$ ) or a laparoscopic partial nephrectomy (LPN,  $n = 18$ ) from August 2008 to January 2011 was undertaken.
- Tumour complexity was stratified into three categories: low (4–6), moderate (7–9) and high (10–12) complexity.
- Complications, and surgical and renal outcomes were recorded and analysed.
- Predictors of conversion to radical nephrectomy (RN) and complications were assessed using univariate and multivariate logistic regression. Multiple linear regression was used to evaluate the prediction of postoperative estimated glomerular filtration rate (eGFR) and warm ischaemia time (WIT).

## Results

- The median RNS was 7 (interquartile range 6–9).
- Tumour complexity was assessed as low in 72 (40.6%), moderate in 87 (49.2%) and high in 18 patients (10.2%).

- There were no significant differences among the three groups with respect to demographic characteristics, operating time, estimated blood loss, transfusion, length of stay, complications and positive surgical margins. Conversion to RN occurred in 29 patients (16.3%).
- RNS was significantly associated with an increased risk of conversion to RN (odds ratio [OR] = 3.5,  $P = 0.01$  and OR = 6.7,  $P = 0.005$ , respectively, for moderate vs low, and high vs low complexity groups).
- On multivariate analysis, RNS was the only independent predictor of WIT ( $P = 0.03$ ) and conversion to RN ( $P = 0.008$ ), but failed to predict postoperative eGFR ( $P = 0.84$ ) and the occurrence of major complications ( $P = 0.91$ ).

## Conclusions

- In the present series, RNS predicted an increased risk of conversion to RN and prolonged WIT.
- RNS was not a predictor of complications and postoperative renal function.

## Keywords

kidney cancer, partial nephrectomy, nephron-sparing surgery, renal tumour

## Introduction

Partial nephrectomy (PN) is considered the standard treatment for most cases of localized renal tumours. Whatever the approach (laparoscopic, open or robotic), oncological results for PN seem to be equivalent to those for radical nephrectomy (RN) [1]. Comparative studies suggest that PN should be performed in all T1, even T1b, tumours [2,3] to decrease morbidity and mortality resulting from renal insufficiency.

The feasibility of a PN depends on the anatomical characteristics of the renal mass and the experience of the surgical team. In addition to tumour size, other anatomical aspects of the tumour are usually considered. Kutikov et al. [4] described a score, the RENAL nephrectomy score (RNS), which was based on characterization of the renal tumour, proposing this as a standardized classification to improve comparability between tumours. Other scores, the PADUA score and C-index, have been described. According to Okhunov et al. [5] all three scores were predictors of warm ischaemia time (WIT) and percent change in postoperative creatinine levels, and Hew et al. [6] showed that the RNS and PADUA were both able to predict the risk of postoperative complications. We chose to evaluate the RNS, as it was the first score used in the literature. The aim of the present study was to determine whether RNS correlates with the surgical outcomes of a PN and postoperative renal function.

## Patients and Methods

### Study Population

We identified, retrospectively, 177 consecutive patients scheduled for PN from August 2008 to January 2011. All patients scheduled for a PN were enrolled. Our institutional review board-approved, prospectively maintained, kidney cancer database was used to identify the study population. Patients were preoperatively staged using CT or MRI. Open PN (OPN) or laparoscopic PN (LPN) was performed by four surgeons, using an extraperitoneal and a transperitoneal approach, respectively.

According to our institutional policy, we treated each patient as conservatively as possible, regardless of tumour size and location. The approach was chosen independently by each surgeon according to his experience. None of the solitary kidneys ( $n = 19$ ) were treated laparoscopically.

### Tumour Assessment

All tumours were classified according to the RNS by the same observer (J.A.L.), who was blinded to the patient's outcome. CT and MRI images were reviewed using axial and coronal reconstructions. The RNS evaluates the tumour size (radius [R]), endophytic or exophytic

properties (E), depth and relationship with the collecting system (nearness [N]), anterior or posterior location (A) and location relative to the polar line (L) [7]. Scores were then stratified into low (4–6), moderate (7–9) and high complexity (10–12) groups.

### Surgical Outcomes

Demographic, clinical, intra-operative and postoperative data included patient age, gender, body mass index (BMI), American Society of Anaesthesiologists (ASA) score, tumour size, RNS, procedure type, estimated blood loss, transfusion rate, WIT, operating time, pathological data, margin status and length of hospital stay. The rate of conversion to RN was also calculated.

Intra- and postoperative complications were stratified using the Clavien–Dindo classification system [8]. Cases of conversion to RN for oncological reasons (macroscopic positive surgical margin or evidence of a non-extirpable tumour) were excluded from the analysis of complications to avoid selection bias. Conversions to RN for intra- or postoperative complications were considered as major complications. Pre- and postoperative renal function was assessed by the preoperative and latest estimated GFR (eGFR) using the Modification of Diet in Renal Disease equation [9].

### Statistical Analysis

Parametric continuous variables are given as the median and interquartile range ([IQR] Q1–Q3). Continuous variables were compared by univariate analysis using Student's *t*-test and the Mann–Whitney *U*-test. Surgical outcomes, including perioperative complications (Clavien–Dindo classification), and renal outcomes were analysed using the Kruskal–Wallis test and Pearson's chi-squared test (with Yates' continuity correction as appropriate). Predictors of conversion to RN and occurrence of major complications were assessed through univariate and multivariate logistic regression. A multiple linear regression was used to evaluate the prediction of postoperative eGFR and WIT. For all statistical analyses, a two-sided *P* value of  $<0.05$  was considered to indicate statistical significance. All data were analysed using R, the free software environment for statistical computing and graphics, version 2.13.1 (2011-07-08).

## Results

Demographic and clinical data are shown in Table 1. The median patient age was 55 (48–66) years. Most patients were male ( $n = 122$ ; 68.9%) and the median tumour size was 31 (20–45) mm. RN was performed in 29 patients (16.4%) including 26 intra-operative conversions to RN for

**Table 1** Demographic data, tumour characteristics, intra-operative and postoperative outcomes in 177 patients.

Variable	Value
Median (IQR) age, years	55 (48–66)
Male, <i>n</i> (%)	122 (68.9)
Median (IQR) BMI, kg/m <sup>2</sup>	25.3 (22.7–27.6)
Right side, <i>n</i> (%)	90 (50.8)
ASA score >3, <i>n</i> (%)	46 (28)
Malignant tumour, <i>n</i> (%)	141 (79.6)
OPN, <i>n</i> (%)	159 (89.8)
Location pole, <i>n</i> (%)	
Lower	72 (40.7)
Mid	58 (32.8)
Upper	47 (26.6)
Median (IQR) tumour size, mm	31 (20–45)
Conversion to RN, <i>n</i> (%)	29 (16.4)
Median (IQR) RNS	7 (6–9)
Complexity group, <i>n</i> (%)	
Low	72 (40.6)
Moderate	87 (49.2)
High	18 (10.2)
RNS location, <i>n</i> (%)	
anterior	80 (45)
posterior	62 (35)
n/a	35 (19.7)
Positive margins, <i>n</i> (%)	3 (1.6)
Median (IQR) operating time, min	135 (120–180)
Blood transfusions, <i>n</i> (%)	31 (17)
Median (range) hospital stay, days	9 (8–11)
Median (IQR) WIT, min	18 (11–25)
Overall complications, <i>n</i> (%)	40 (22.6)
Minor	18 (10.1)
Major	22 (12.4)
Surgical complications, <i>n</i> (%)	22 (12.4)
Medical complications, <i>n</i> (%)	18 (10.2)
Median (IQR) preoperative eGFR, mL/min/1.73 m <sup>2</sup>	77.4 (63.3–90.9)
Median (IQR) postoperative eGFR, mL/min/1.73 m <sup>2</sup>	55.5 (49.6–69.3)

uncontrolled bleeding (*n* = 2) and for oncological reasons (*n* = 24). Three RNs had to be performed postoperatively because of uncontrolled bleeding (*n* = 1), a renal artery thrombosis (*n* = 1) and a persistent urinary leak after failure of ureteric stent placement (*n* = 1). All RNs performed were referred to as conversions to RN. On univariate analysis (Table 2), patients undergoing RN had larger tumours (median size 4.0 vs 3.0 cm; *P* = 0.006) and a higher RNS (8 vs 7; *P* = 0.006). A laparoscopic approach was not correlated with a higher risk of conversion to RN (*P* = 0.5); conversions to RN were performed in 13.8% of LPN cases and in 15.8% of OPN cases. The stratification of RNS into three complexity groups showed a correlation with an increasing risk of conversion to RN (odds ratio [OR] = 3.5, *P* = 0.01 when comparing moderate vs low complexity groups and OR = 6.7, *P* = 0.005 for high vs low complexity groups).

Major complications were assessed after excluding patients undergoing conversion to RN for oncological reasons. Patients developing major complications had a significantly higher BMI (24.9 vs 27.6 kg/m<sup>2</sup>, *P* < 0.001) and a significantly higher rate of malignant tumours (95.2% vs

75.8%, *P* = 0.047). No statistical difference was found in RNS or complexity group among patients developing major complications or not (Table 3). On multivariate analysis, after adjusting for BMI and histology, RNS as a continuous variable failed to predict the occurrence of major complications (OR = 0.98, 95% CI 0.75–1.29, *P* = 0.906). Complexity group also failed to predict an increased risk of major complications (OR = 0.77, 95% CI 0.27–2.2, *P* = 0.622 for moderate vs low complexity groups and OR = 1.86, 95% CI 0.41–8.57, *P* = 0.424 for high vs low complexity groups).

On multivariate linear analysis adjusting for ASA score ( $\beta$  = –0.648, 95% CI –3.85–2.55, *P* = 0.69) and laparoscopic approach ( $\beta$  = 0.67, 95% CI: –6.68–10.4, *P* = 0.67), RNS was the only predictor of WIT ( $\beta$  = 5.89, 95% CI 2.045–9.75, *P* = 0.03). Postoperative eGFR was not predicted by RNS. The only independent predictors of postoperative eGFR were preoperative eGFR and ASA score (Table 4). Complexity group was an independent predictor of conversion to RN, especially for the low vs moderate complexity group (Table 5).

## Discussion

The anatomical characterization of a renal tumour before surgical treatment has long lacked standardization. Since the study by Patard et al. [1], tumour size defined by its diameter has no longer been a limiting factor: elective PN can be safely and effectively performed for tumours up to 7 cm.

The first anatomical characterization to evaluate the predicted difficulty of a PN was published by Kutikov and Uzzo [7]. The objective of this integrated anatomical system was to predict the oncological feasibility of a PN using a classification based upon criteria that every surgeon considered separately before surgery. They intended to standardize descriptions of renal masses and allow meaningful comparisons.

In the present retrospective review of 177 patients scheduled for PN, the RNS was correlated with renal mass complexity as measured by the rate of conversion to RN and WIT. Based on this information, surgeons can optimize patient care by choosing the most appropriate approach and by eventually referring the patient to a high-volume centre.

We reported higher rates of conversion to RN (16.4%) than those reported in other previously published series. Galvin et al. [10] reported a rate of 6% in a recent study. This difference may be explained by the high rate of intra-operative conversions to RN for oncological reasons (*n* = 82, 7%) in the present study, resulting from a systematic attempt to be as conservative as possible, independent of tumour size and location.

**Table 2** Conversion to RN.

<b>Patient characteristic, N = 177</b>	<b>Conversion to RN, n = 29</b>	<b>PN success, n = 148</b>	<b>P</b>
Median (SE) age	57.9 (24.6)	55.0 (25.77)	0.25
Male, n (%)	20 (69)	102 (69)	0.83
Median (IQR) BMI, kg/m <sup>2</sup>	26.7 (24.1–27.6)	25.2 (2.7–27.4)	0.11
Right side, n (%)	17 (58.6)	73 (49.3)	0.47
Laparoscopy, n (%)	4 (13.8)	14 (9.5)	0.5
ASA score, n (%)			0.82
1	6 (20.7)	46 (31.8)	
2	10 (34.5)	56 (37.8)	
3	7 (24.1)	39 (26.3)	
Malignant tumour, n (%)	26 (89.6)	115 (77.7)	0.22
Size, mm	40 (30–55)	30 (20–40)	<b>0.006*</b>
Location, n (%)			0.52
Lower pole	14 (48.3)	58 (39.2)	
Mid	7 (24.1)	51 (34.5)	
Upper pole	8 (27.6)	39 (26.3)	
RNS	8 (7–9)	7 (6–8)	<b>0.006*</b>
RNS location, n (%)			0.44
anterior	10 (34.5)	70 (47.3)	
posterior	12 (41.4)	50 (33.8)	
n/a	7 (24.1)	28 (18.9)	
Complexity group, n (%)			<b>0.008*</b>
Low	5 (17.2)	67 (45.3)	
Moderate	18 (62)	69 (46.6)	
High	6 (20.7)	12 (8.1)	
Median (SE) postoperative eGFR	49.22 (14.7)	61.48 (21.35)	<b>0.02*</b>

\*Statistically significant.

**Table 3** Univariate analysis of occurrence of major complications (excluding patients who underwent RN for oncological reasons).

<b>Patient characteristic, N = 153</b>	<b>No major complication (Clavien 0–2), n = 132</b>	<b>Major complication (Clavien 3–4), n = 21</b>	<b>P</b>
Median (IQR) age	56 (47–63.2)	55 (52–67)	0.40
Male, n (%)	90 (68.7%)	17 (80.9%)	0.31
Median (IQR) BMI, kg/m <sup>2</sup>	24.9 (22.3–27.2)	27.6 (26.5–28.3)	<b>&lt;0.001*</b>
Right side, n (%)	68 (51.5)	9 (42.8)	0.49
Laparoscopy, n (%)	11 (8.3)	4 (19)	0.13
ASA score, n (%)			0.46
1	52 (39.4)	9 (42.9)	
2	45 (34.1)	6 (28.6)	
3	35 (26.5)	6 (28.6)	
Malignant tumour, n (%)	100 (75.8)	20 (95.2)	<b>0.047*</b>
Median (IQR) tumour size, mm	30 (20–40)	33.50 (23.7–42)	0.67
Location, n (%)			0.88
Lower pole	52 (39.4)	9 (42.8)	
Mid	45 (34.1)	6 (28.6)	
Upper pole	35 (26.5)	6 (28.6)	
Median (IQR) RNS	7 (6–8)	7 (5–9)	0.86
RNS location, n (%)			0.55
anterior	60 (45.4)	12 (57.1)	
posterior	46 (34.8)	5 (23.8)	
n/a	46 (34.8)	4 (19.1)	
Complexity group, n (%)			0.51
Low	59 (44.7)	10 (47.6)	
Moderate	63 (47.7)	8 (38.1)	
High	10 (7.6)	3 (14.3)	

\*Statistically significant.

**Table 4** Multivariate linear analysis for prediction of postoperative eGFR.

	<b>Coefficient</b>	<b>95% CI</b>	<b>P</b>
RNS	0.098	-2.73; 8.67	0.84
ASA score	-0.254	-17.07; -2.12	0.013*
Approach (LPN vs OPN)	-0.198	-30.08; 0.98	0.064
WIT	0.012	-0.29; 0.34	0.34
Preoperative eGFR	0.75	0.45; 0.77	<0.001*

\*Statistically significant.

**Table 5** Multivariate logistic regression analysis for prediction of conversion to RN.

<b>Variable</b>	<b>OR</b>	<b>95% CI</b>	<b>P</b>
RNS groups			0.008*
Intermediate vs low	0.78	0.15-0.41	0.03*
High vs low	0.473	0.14-1.61	0.23
Laparoscopy vs open	0.32	0.06-1.56	0.16
BMI	1.18	0.96-1.24	0.15
ASA score	1.38	0.47-4.06	0.62
Malignant vs benign tumour	0.44	0.31-0.44	0.44

\*Statistically significant.

In the present series, the RNS was not a predictor of major complications. We chose to exclude from the analysis of complications these cases of intra-operative conversion to RN to avoid minimizing our complication rate after RN. We described an overall complication rate comparable with previously published series. Porpiglia et al. [11] reported an overall complication rate of 21.4% in their review. We chose to focus only on major complications because of their clinical significance, in that they prolong hospital stay and induce long-term morbidity or potential mortality.

The present findings contrast with previous studies by Rosevear et al. [12] who described a higher RNS among patients developing complications, and Simhan et al. [13] who reported that RNS complexity groups were associated with the occurrence of major complications. Hew et al. [6] found no correlation between the intermediate complexity group and the complication rate, but high complexity group did predict an increased risk of complications.

In the present series, the variables that correlated with an increased risk of complications were BMI and tumour malignancy. After adjusting for these two variables, RNS still failed to predict major complications. This might be explained by the insufficient statistical power of the present study, given the low frequency of complications and our choice to only take into account the less frequent major complications. However, the rate (12.4%) of major complications (Clavien 3 and 4) in the present series remains high compared with previous studies. Retrospectively, it is difficult to know what could explain

our high rate. On multivariate analysis, the laparoscopic approach was not found to be associated with major complications; however, although it did not reach significance, we noted that major complications occurred in 19% of LPNs. We believe that in the present series, laparoscopy could have increased our major complication rate.

We found that RNS was an independent predictor of WIT but failed to show a correlation with postoperative eGFR in multivariate linear analysis. Preoperative renal function in our series was low (77.4 mL/min/1.73 m<sup>2</sup>). This could be related to comorbidities of the patients and the high number of solitary kidneys. To adjust for this confounding factor, preoperative eGFR was included in the multivariate model predicting postoperative eGFR.

Only few studies report a link between anatomical features of the tumour and postoperative renal function, Okhunov et al. [5] reported that RNS was associated with percent change in creatinine level. The assessment of RNS requires the use of coronal reconstructions to define the polar lines limiting the sinus, according to Kutikov and Uzzo [7], but the images, particular those from MRI, are not always suitable. Moreover, designation of anterior or posterior location is not always feasible because of the lack of a clear demarcation of the lateral peritoneal reflection. In the present study, on univariate analysis, anterior or posterior locations were not associated with a higher rate of conversion to RN or the occurrence of major complications. Measuring the distance between the tumour and the urinary collecting system also appears complex and hardly reproducible.

Recently, Ficarra et al. [14] published a series describing the PADUA classification. Compared with the RNS, their score has the advantage of defining the sinus borders as the first slides that show the presence of adipose tissue, allowing the use of only axial images. We believe the main difference between these two scores in favour of PADUA classification is the absence of determination of the distance between the urinary collecting system and the tumour: PADUA classification only considers the involvement of the sinus or the pelvicalyceal system. The C-index, described by Simmons et al. [15], is another method of quantifying the proximity of kidney tumours to the renal central sinus.

Recently, Okhunov et al. [5] compared the three scores described above in 101 patients. All scores were predictors of WIT and percent change in creatinine level; however, they failed to predict the occurrence of complications.

Using a standardized classification for renal tumours is a major step towards an objective comparison of the indications and expected outcomes of PN. We believe that the results of emerging laparoscopic and robotic

techniques should be evaluated in light of these tumour classifications.

The present study has several limitations. Because of its retrospective nature, complications may have been omitted. Our prospectively maintained database reduces this risk, however, and complications not recorded are more likely to be minor. The evaluation of postoperative eGFR is limited by a relatively short follow-up because most patients were followed in their referring hospitals after surgery. Choosing to include all patients independently of the approach may also have influenced the results. Few studies report that functional and early oncological outcomes were similar in laparoscopic and open approaches; in fact, LPN was associated with additional postoperative morbidity compared with OPN [16]. Retrospectively in the present study, it is difficult to know whether the patients who finally underwent a laparoscopic RN could have benefited from an open conversion rather than a conversion to laparoscopic RN. Among patients who lost their kidney, most of them had hilar involvement or an insufficient residual kidney volume. Since OPN is still considered a standard of care, we recommend to convert to open these patients rather than perform a LPN. Most patients underwent OPN because LPN still represents a challenging procedure requiring a long learning curve but, on multivariate analysis, no significant difference in surgical outcome was found between laparoscopic and open approaches.

Another limitation is the difference in surgeon's experience, which was not evaluated in the present study. In addition, we deliberately chose not to disclose intermediate- and long-term oncological outcomes, as our goal was not to correlate RNS with oncological outcomes.

In the present series, RNS was able to predict the surgical difficulty of a PN by predicting the risk of conversion to RN and longer WIT; however, the score failed to predict the occurrence of major complications and postoperative renal function.

## Conflict of Interest

None declared.

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**Abbreviations:** RNS, RENAL nephrectomy score; PN, partial nephrectomy; OPN, open PN; LPN, laparoscopic PN; RN, radical nephrectomy; eGFR, estimated GFR; WIT, warm ischaemia time; OR, odds ratio; BMI, body mass index; ASA, American Society of Anaesthesiologists.

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