A novel nephrometry scoring system for predicting peri-operative outcomes of retroperitoneal laparoscopic partial nephrectomy

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Abstract

Background: Although the impact of tumor complexity on peri-operative outcomes has been well established using several nephrometry scoring systems, the impact of adherent perirenal fat remains poorly defined. This study aimed to develop a novel nephrometry scoring system for predicting the peri-operative outcomes of laparoscopic partial nephrectomy (LPN) by integrating and optimizing the RENAL score (RNS) and Mayo adhesive probability (MAP) score.

Methods: We retrospectively evaluated 159 patients treated with retroperitoneal LPN. The patients' demographic parameters, RNSs, and MAP scores were evaluated as potential predictors of perioperative outcomes, including operation time, estimated blood loss (EBL), and margin, ischemia, and complication (MIC) achievement rate. The independent predictors were used to develop a novel nephrometry scoring system. The predictive value and inter-observer agreement for the novel nephrometry scoring system were evaluated.

Results: Tumor radius (R score), nearness to the renal sinus or collecting system (N score), and posterior perinephric fat thickness were independent predictors of peri-operative outcomes and were used to develop the RNP score. The univariate analysis revealed that the RNP score was significantly associated with operation time, EBL, and MIC achievement rate ($P < 0.050$). The RNP score was an independent predictor of operation time ($P < 0.001$), EBL ($P = 0.018$), and MIC achievement rate ($P = 0.023$) in the multivariate analysis. The RNP score was not inferior to RNS in the area under the curve for predicting peri-operative outcomes and performed better in inter-observer agreement (76.7% *vs*. 57.8%) and kappa value (0.804 *vs*. 0.726).

Conclusion: The RNP score, combining the advantages of the RNS and MAP score, demonstrated a good predictive value for the peri-operative outcomes of retroperitoneal LPN and better inter-observer agreement.

Keywords: Laparoscopy; Nephrectomy; RENAL score; Mayo adhesive probability score

Introduction

Renal cell carcinoma (RCC), which has high surgical complexity, is associated with a higher complication rate and longer warm ischemia time (WIT) in partial nephrectomy (PN). Therefore, several scoring systems have been developed to quantify tumor complexity, predict outcomes of PN, and aid patient selection, such as the RENAL score (RNS),[1] PADUA score,[2] and Diameter-axial-polar (DAP) score.[3] The importance of these nephrometry scoring systems in predicting the perioperative outcomes of PN has been demonstrated.

Tumor- and patient-related factors may add to the technical complexity of PN.[4] However, the existing scoring systems all focus on the anatomical characteristics of the tumor itself. They do not take into account the impact of patient-related characteristics on surgical complexity and perioperative outcomes. One of the most notable patient-specific factors is adherent perinephric fat (APF) characterized by inflammatory adipose tissue surrounding the kidney, which increases the surgical difficulty and makes mobilizing and isolating the tumor challenging.[5] Both the density and thickness of perinephric fat have been associated with surgical complexity and peri-operative outcomes. Davidiuk *et al*[6] developed the Mayo adhesive probability (MAP) scoring system based on posterior perinephric fat thickness and stranding, which can accurately predict the presence of APF.[7]

In the present study, we systematically evaluated the association of each component of RNS and MAP score with perioperative outcomes of retroperitoneal laparo-

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scopic partial nephrectomy (LPN). We aimed to develop a novel nephrometry scoring system by integrating and optimizing the RNS and MAP score, and to evaluate its predictive value and inter-observer agreement.

Methods

Ethics approval

This study was approved by the Peking University Third Hospital Medical Science Research Ethics Committee (No. IRB00006761-M2018265), and all research procedures were performed in accordance with the relevant regulations. As a retrospective study and data analysis was performed anonymously, this study was exempt from informed consent from patients.

Patient selection

We reviewed the clinical records of 159 consecutive patients who underwent retroperitoneal LPN between January 2015 and August 2016, met the inclusion criteria for single cT1 RCC, and had pre-operative computerized tomography (CT) scans available. The exclusion criteria included congenital kidney malformation, isolated kidney, coagulation dysfunction, and history of abdominal operation or radiofrequency ablation. A standard retroperitoneal LPN was performed for all the patients as previously described.[8]

The demographic parameters and perioperative data were recorded, including age, sex, body mass index (BMI), previous history, American Society of Anesthesiologists (ASA) score, operative time, estimated blood loss (EBL), WIT, and margin and post-operative complications. Two pathologists reviewed the tumor tissue samples to double-check the criterion for a positive surgical margin. Post-operative complications were defined as those occurring within 30 days after LPN and were evaluated in accordance with the Clavien-Dindo classification. Margin, ischemia, and complications (MIC) achievement rate was acquired when the surgical margins are negative, the WIT was <20 min, and no major complications (Clavien III/IV) were observed.[9]

Radiological evaluation

The RNS was evaluated as described by Kutikov *et al*.[1] Tumor radius (R score), exophytic/endophytic property (E score), nearness to the renal sinus or collecting system (N score), and location relative to polar lines (L score) were assessed on a three-point scale. The MAP score was evaluated as described by Davidiuk *et al*.[6] Fat thickness was measured at the level of the renal vein on the ipsilateral side of the RCC. The posterior perinephric fat thickness was measured from the renal capsule to the posterior abdominal wall (<1.0 cm = 0 point, 1.1–1.9 cm = 1 point, ≥2.0 cm = 2 points). The stranding score was acquired at the same level (no stranding = 0 points, mild/moderate stranding = 2 points, severe stranding = 3 points).

The measurements were performed by one radiologist (Scorer A), one urologist (Scorer B), and one senior radiologist (Scorer C). Before the formal analysis, five measurements were performed to acquaint the scorers with the proper methodology and technique for the two scoring systems. Scorers A and B, blinded to the peri-operative outcomes, independently calculated the RNS and MAP score based on the pre-operative CT scan. Scorer C recalculated the components with disagreement between scorers A and B to acquire the final scores.

Statistical analysis

The association of each component of the RNS and MAP score with the peri-operative outcomes were evaluated using the uni-multivariate regression analysis. Comparisons of the peri-operative outcomes according to the novel nephrometry category were evaluated using the Kruskal-Wallis *H* test or Chi-square test. A multivariate regression analysis was used to quantify the predictive value of the novel nephrometry scoring system. Receiver-operating characteristic curves were generated for the novel nephrometry scoring system; and RNS and MAP score, to predict the operative time, EBL, and MIC achievement rate. The areas under the curve (AUC) were compared using the method proposed by Delong *et al*.[10] Kappa values were used to evaluate the inter-observer agreement. All statistical tests were two-sided, and a P value of <0.05 was considered statistically significant. Analyses were performed with SPSS v.22.0 (IBM Corp, Armonk, NY, USA).

Results

Baseline characteristics

The clinical and radiological data of the included patients are summarized in Table 1. The median (interquartile range) RNS, MAP score, operative time, EBL, WIT, and MIC achievement rate were 8 (6–9), 1 (0–3), 149 min (116–186 min), 20 mL (10–50 mL), 25 min (18–30 min), and 27.0% (43%–159%), respectively.

Association of each component with the peri-operative outcomes

In the univariate linear regression analysis, operative time was significantly associated with sex, age, BMI, cardiovascular disease, hypertension, ASA score, R score, N score, posterior perinephric fat thickness, and stranding. Only R score ($B = 24.753$ [5.163–44.344], $P = 0.014$), N score ($B = 10.183$ [0.784–19.582], $P = 0.034$), and posterior perinephric fat thickness ($B = 16.536$ [3.436–29.636], $P = 0.014$) were the independent predictors of operative time in the multivariate analysis [Supplementary Table 1, http://links.lww.com/CM9/A171].

In the multivariate analysis, only R score ($B = 34.964$ [1.835–68.093], $P = 0.039$) was an independent predictor of EBL, and only N score (odds ratio [OR] = 0.627 [0.397–0.992], $P = 0.046$) was an independent predictor of MIC achievement rate [Supplementary Tables 2 and 3, http://links.lww.com/CM9/A171].

Table 1: Clinical and radiological characteristics of 159 consecutive patients who underwent retroperitoneal laparoscopic partial nephrectomy.

Characteristics	Values
Sex, *n* (%)	
Female	112 (70.4)
Male	47 (29.6)
Age (years), median (IQR)	52 (45–61)
Body mass index (kg/m^2), median (IQR)	25.1 (22.9–27.2)
Cardiovascular disease, *n* (%)	14 (8.8)
Hypertension, *n* (%)	54 (34.0)
Diabetes, *n* (%)	27 (17.0)
Dyslipidemia, *n* (%)	60 (37.7)
Smoking history, *n* (%)	24 (15.1)
ASA classification, *n* (%)	
Score 1	35 (22.0)
Score 2	116 (73.0)
Score 3	8 (5.0)
Tumor size (mm), median (IQR)	29.4 (21.5–36.0)
Clinical T stage, *n* (%)	
T1a	133 (83.6)
T1b	26 (16.4)
Operative time (min), median (IQR)	149 (116–186)
Estimated blood loss (mL), median (IQR)	20 (10–50)
Warm ischemia time (min), median (IQR)	25 (18–30)
Post-operative complication, *n* (%)	
Clavien I	54 (34.0)
Clavien II	3 (3.9)
Clavien III/IV	0
Positive surgical margin, *n* (%)	10 (6.3)
MIC achievement rate, *n* (%)	43 (27.0)
RENAL score, median (IQR)	8 (6–9)
Mayo adhesive probability score, median (IQR)	1 (0–3)

IQR: Interquartile range; eGFR: Estimated glomerular filtration rate; MIC: Margin, ischemia, and complications.

Predictive value of the RNP score

The R score, N score, and posterior perinephric fat thickness had the highest predictive values for perioperative outcomes. The R score (≤4 cm = 1 point, >4 but <7 cm = 2 points, ≥7 cm = 3 points), N score (≥7 mm = 1 point, >4 but <7 mm = 2 points, ≤4 mm = 3 points), and posterior perinephric fat thickness (≤1.0 cm = 1 point, 1.1–1.9 cm = 2 points, ≥2.0 cm = 3 points) were assessed on a three-point scale. They were therefore used to develop a novel nephrometry scoring system, termed RNP score, with scores ranging from 3 to 9 [Table 2]. The patients were stratified into low (3–4), moderate (5–6), and high (7–9) complexity groups based on the RNP score.

The RNP score category was significantly associated with operative time (χ^2 = 25.137, P < 0.001), EBL (χ^2 = 21.661, P < 0.001), WIT (χ^2 = 11.153, P = 0.004), and MIC achievement rate (χ^2 = 6.957, P = 0.031) [Table 3]. In the multivariate analysis, the RNP score was an independent predictor of operative time (B = 17.749 [8.094–27.404], P < 0.001), EBL (B = 20.725 [3.594–37.857], P = 0.018), and MIC achievement rate (OR = 0.523 [0.299–0.916], P = 0.023) [Table 4].

Table 2: Definition of RNP score.

Items	1 point	2 points	3 points
Radius (cm)	≤4	>4 but <7	≥7
Nearness of the tumor to the collecting system or sinus (mm)	≥7	>4 but <7	≤4
Posterior perinephric fat thickness (cm)	<1.0	1.1–1.9	≥2.0

We compared the AUC for operative time of >150 min, EBL of >20 mL, and MIC achievement rates of the RNP score, RNS, and MAP score [Figure 1]. Compared with the RNS, the RNP score had a higher AUC for operative time of >150 min (0.697 *vs*. 0.569, P = 0.004), and EBL of >20 mL (0.701 *vs*. 0.591, P = 0.014), and a comparable AUC for MIC achievement (0.633 *vs*. 0.626, P = 0.907). Compared with the MAP score, the RNP score had a higher AUC for EBL of >20 mL (0.701 *vs*. 0.606, P = 0.011) and MIC achievement (0.633 *vs*. 0.526, P = 0.008), and a comparable AUC for operative time of >150 min (0.697 *vs*. 0.655, P = 0.260).

Inter-observer agreement of the RNP score

The inter-observer agreements for R score, E score, N score, L score, posterior perinephric fat thickness and stranding, RNS, MAP score, and RNP score were 99.4%, 84.9%, 80.5%, 77.3%, 91.2%, 82.4%, 57.8%, 76.7%, and 76.7%, respectively, corresponding to kappa values of 0.975, 0.770, 0.693, 0.750, 0.883, 0.585, 0.726, 0.728, and 0.804, respectively. The RNP score showed better inter-observer agreement than the RNS.

Discussion

We developed a simple RNP score by integrating the optimized attributes of the RNS and MAP score to evaluate the perioperative outcomes of retroperitoneal LPN. The RNP score takes into consideration the internal characteristics and external environment of the tumor. In our study, the R score, N score, and posterior perinephric fat thickness correlated well with the perioperative outcomes of LPN. The RNP score independently predicted the risk of increased operation time, EBL, and WIT, and decreased MIC achievement rate. The RNP score, which includes only three quantitative components, is objective and simple to evaluate based on enhancement CT.

The RNS has been demonstrated to be associated with surgical complexity and outcomes of PN in many validation studies.[11,12] However, few reports have indicated that the accuracy of the RNS in predicting outcomes and reproducibility is inconsistent, hindering its universal applicability.[13,14] The RNS was reported as a quantitative score and then as a descriptive score, preventing us from intuitively and comprehensively understanding the score. According to the results of Spaliviero *et al*,[15] only the R, N, and L scores were useful for predicting the peri-operative outcomes of PN. In a critical appraisal of the RNS, only the R and N scores were

Table 3: Perioperative outcomes of 159 patients who underwent retroperitoneal laparoscopic partial nephrectomy according to RNP score category.

Items	RNP score category				
	Low (3–4) (*N* = 33)	Moderate (5–6) (*N* = 96)	High (7–9) (*N* = 30)	χ^2	*P*
Operative time (min)	125 (106–156)	142 (116–179)	213 (157–237)	25.137	**<0.001**
Estimated blood loss (mL)	10 (10–20)	20 (13–50)	50 (30–100)	21.661	**<0.001**
Warm ischemia time (min)	19 (15–30)	25 (19–30)	30 (23–40)	11.153	**0.004**
Post-operative complication	7 (21.2)	35 (36.5)	15 (50.0)	5.861	0.053
Positive surgical margin	4 (12.1)	5 (5.2)	1 (3.4)	2.194	0.334
MIC achievement rate	14 (42.4)	25 (26.0)	4 (13.3)	6.957	**0.031**

Values were shown as median (IQR), or *n* (%). IQR: Interquartile range; MIC, Margin, ischemia, and complication.

Table 4: Multivariate regression analysis of operative outcomes among 159 consecutive patients who underwent retroperitoneal laparoscopic partial nephrectomy.

Items	Operative time		Estimated blood loss		MIC achievement	
	B (95% CI)	*P*	*B* (95% CI)	*P*	OR (95% CI)	*P*
Sex	10.051 (−13.820 to 33.923)	0.407	24.147 (−18.212 to 66.505)	0.262	0.452 (0.116–1.768)	0.254
Age	−0.138 (−0.865 to 0.590)	0.709	0.954 (−0.337 to 2.245)	0.146	1.003 (0.962–1.045)	0.893
BMI	1.408 (−0.901 to 3.716)	0.230	0.275 (−3.821 to 4.372)	0.894	1.060 (0.931–1.206)	0.377
RNP score	17.749 (8.094–27.404)	**<0.001**	20.725 (3.594–37.857)	**0.018**	0.523 (0.299–0.916)	**0.023**
RNS	−1.985 (−7.492 to 3.522)	0.477	−0.686 (−10.457 to 9.086)	0.890	0.918 (0.669–1.259)	0.594
MAP score	−0.735 (−8.118 to 6.648)	0.844	−9.445 (−22.546 to 3.655)	0.156	1.253 (0.802–1.958)	0.321

B, odds ratio, 95% CI, and *P* values resulted from a regression model adjusted for RNP score, RENAL score, Mayo adhesive probability score, sex, age, body mass index (BMI), cardiovascular disease, hypertension, diabetes, dyslipidemia, smoking history, American Society of Anesthesiologists score, pre-operative hemoglobin level, and pre-operative estimated glomerular filtration rate. MIC: Margin, ischemia, and complications; CI: Confidence interval; OR: Odds ratio; RNS: RENAL score; MAP: Mayo adhesive probability.

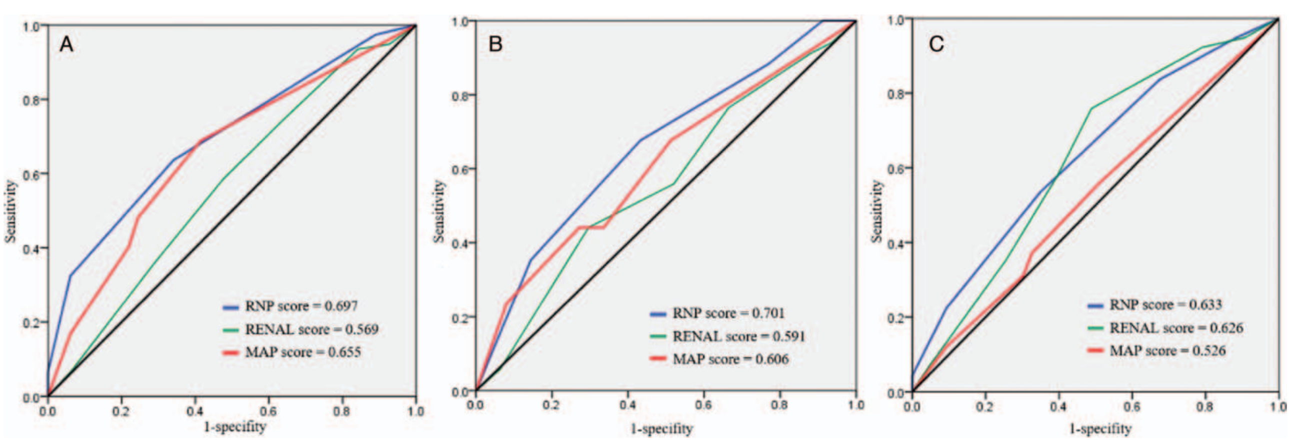

Figure 1: Area under the curve of the RNP score, RENAL score, and Mayo adhesive probability score for predicting (A) operative time of >150 min, (B) EBL of >20 mL, and (C) MIC achievement. EBL: Estimated blood loss; MIC: Margin, ischemia, and complications; ROC: Receiver-operating characteristic.

found to be predictors of complexity in the multivariate analysis.[16] In our study, E score failed to show a significant association with operation time, EBL, or MIC achievement rate in both the univariate and multivariate analyses. With the widespread use of intra-operative ultrasonography, the importance of the convexity rate is decreasing. The contribution of the E score to the RNS deserves careful consideration. Some modified scoring systems were developed to overcome the limitations,[2,3] but no superiority to RNS was demonstrated.[12,16] Chinese urologists prefer the retroperitoneal approach for LPN that has considerable convenience for anterior and posterior tumors. In our study, LPN was performed using the retroperitoneal approach. Therefore, we did not include the data for the anterior/posterior tumors in the multivariate analysis.

A recent report has shown that RNS, MAP score, and patient-related factors all had some influence on peri-operative outcomes.[4] The existing nephrometry scoring systems were designed to evaluate the characteristics of the tumor itself, but they all neglected the environment- and patient-related factors that may cause increased surgical complexity and morbidity, particularly APF. The incidence of APF during PN varies greatly in reported studies. Two large prospective studies reported APF incidence rates of 30% and 40.8%, respectively.[5,17] The presence of APF can be an obstacle to mobilizing the kidney tumor and isolate the renal hilum, and its removal can often lead to tearing of the renal capsule. Reports have demonstrated that the presence of APF correlated with increased operative time and EBL, but not WIT and the incidence rates of peri-operative complications and surgical margins.[5,17,18] Some authors found that the presence of APF may be associated with malignant renal histology.[18] Khene *et al*[19] investigated 202 patients who underwent robot-assisted PN, and their result showed that the presence of APF caused significant increases in operative time, EBL, and conversion rate, and resulted in more transfusions.

APF is an important factor that affects the perioperative outcomes of PN. The difficulty to deal with APF may compel less-experienced surgeons to select RN or percutaneous ablation to treat RCC. However, the presence of APF is difficult to accurately predict using clinical and imaging data before operation. Zheng *et al*[20] found that the perinephric fat surface density was higher in APF and showed a significant ability to predict the difficulty of perinephric fat surgical dissection (AUC = 0.87, $P < 0.001$). CT texture analysis was supported to be a promising quantitative imaging tool to help urologists identify APF.[21] However, the variables of the methods may be difficult to measure in a time-efficient manner, particularly in the clinical setting. Davidiuk *et al*[6] developed a simple scoring system termed MAP score to predict the presence of APF. Several studies have demonstrated the ability of MAP score to predict APF.[5-7] Other tumor characteristics such as central and hilar locations may lead to surgical challenges in tumor excision and kidney reconstruction. Therefore, these anatomical characteristics must be taken into account during assessment of the complexity of LPN. A study by Dulabon *et al*[22] represents a largest series of renal hilar tumors and suggested that PN is a safe and feasible option for renal hilar tumors. However, a significant increase in WIT was observed in the hilar group as compared with the non-hilar group, even in the hands of experienced surgeons.[22] Furthermore, renal anatomical variants such as multiple renal arteries, solitary kidney, and horseshoe kidney may increase the surgical complexity of LPN.

Our study integrated the parameters of tumor and perinephric fat to predict the outcomes of PN, the RNP score showed higher predictive values for surgical complexity and MIC achievement rate than the RNS and MAP score, respectively. The main innovations of the RNP score are the introduction of posterior perinephric fat thickness and the simplification of the RNS. High measurement variability restricts the promotion of current nephrometry systems. Our findings demonstrate a substantial-to-almost perfect agreement for the individual components and RNP scores between a radiologist and urologist. The best results were found for the R score and posterior perinephric fat thickness. Stranding showed the worst agreement. In our study, the RNP score showed better agreement than the RNS. Our results suggest the RNP score to be a promising scoring system for predicting the outcomes of PN. External validation of the RNP score in renal tumors treated with LPN is necessary in the future.

Our study also had some limitations. The retrospective nature of our study and the patient selection process may have generated unanticipated biases. Some patients were excluded owing to the absence of pre-operative CT scans and the choice of transperitoneal LPN. In addition, the analysis results were based on the final data re-scored by scorer C, lacking an independent analysis of the data from scorers A and B. Finally, LPN was performed by surgeons with various levels of surgical experience, which may have impacted the peri-operative outcomes but was not adjusted for.

In conclusion, we found that the R score, N score, and posterior perinephric fat thickness were the most important determinants of perioperative outcomes. The RNP score is a promising scoring system for predicting perioperative outcomes, with substantial inter-observer agreement. We believe that the RNP score can be useful in the decision making by urologists regarding the management of renal tumors.

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Conflicts of interest

None.

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