Published in final edited form as:

Urol Oncol. 2015 March ; 33(3): 112.e9–112.e14. doi:10.1016/j.urolonc.2014.11.003.

Preoperative Predictors of Malignancy and Unfavorable Pathology for Clinical T1a Tumors Treated with Partial Nephrectomy: A Multi-Institutional Analysis

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Abstract

Purpose—To determine preoperative predictors associated with RCC and unfavorable pathology in small renal masses treated with partial nephrectomy (PN).

Materials and Methods—PN records from 5 centers were retrospectively queried for patients with a clinically localized, single tumor < 4 cm on imaging (cT1a). Between 2007 and 2013, 1009 patients met inclusion criteria. Unfavorable pathology was defined as any grade III or IV RCC or tumors upstaged to pathologic T3a disease. Logistic regression models were used to determine preoperative characteristics associated with RCC and with unfavorable pathology.

Results—A total of 771 (76.4%) patients were found to have RCC and 198 (19.6%) had unfavorable pathology. On multivariate, bootstrap-adjusted logistic regression analysis, factors associated with presence of malignancy were imaging tumor size > 3 cm (OR 1.46, $p = 0.040$), male sex (OR 1.88, $p < 0.0001$) and nephrometry score > 8 (OR 1.64, $p = 0.005$). These same factors were independently associated with risk of unfavorable pathology: size > 3 cm (OR 1.46, $p = 0.021$), male sex (OR 2.35, $p < 0.0001$) and nephrometry score > 8 (OR 1.49, $p = 0.015$). The c statistic was 0.62 for the predicting malignancy and 0.63 for unfavorable pathology.

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Conclusions—In this multi-institutional cohort, male sex, imaging tumor size >3 cm, and nephrometry score >8 were predictors of RCC and adverse pathology following PN. These factors may assist in risk stratification and selective renal mass biopsy prior to decision making. Further studies are necessary to validate these findings.

Keywords

Renal cell carcinoma; partial nephrectomy; risk stratification

1. Introduction

The incidence of renal cell carcinoma (RCC) has increased over the last several decades, driven by the incidental detection of small renal masses (SRM)s, tumors 4 cm or less, on cross-sectional imaging [1]. The majority of patients diagnosed with a SRM will ultimately undergo an extirpative surgery; however at final pathology 20-30 % of SRMs are found to be benign [2]. Even the majority of tumors that are found to be cancer are low-grade and of low-malignant potential [3]. Current risk stratification is clearly imperfect.

Currently, there are no urine or serum diagnostic markers for RCC. The utilization of renal mass biopsy (RMB) has increased in recent years and historic concerns about safety and biopsy tract seeding appear to be greatly diminished in contemporary series [4, 5]. However, the accuracy of RMB for detecting high- grade and potentially aggressive tumors continues to be limited [6, 7]. Pre-operative nomograms based on patient characteristics and radiographic features are an attractive means of risk stratification. Existing nomograms were constructed from datasets that contain a high proportion of larger tumors that have different biologic potential than SRMs, and the utility of these nomogram for patients with SRMs may be limited [8-11].

Because of the lack of a prognostic instrument designed specifically for SRMs, we sought to build a predictive tool built for patients with SRMs that utilized simplified risk tables to predict the chance of malignancy and unfavorable pathology for clinical T1a lesions amenable to partial nephrectomy.

2. Methods

2.1 Patient Selection

A prospectively-maintained, institutional review board-approved robotic PN registry including patients from 5 institutions (Johns Hopkins, Washington University, Cleveland Clinic, New York University, and Henry Ford) was queried for PN performed for organ-confined kidney tumors 4 cm (clinical T1a) between May 2007 and August 2013. Patients with multiple tumors, known or suspected metastases were excluded. A total 1,098 PN were performed for solitary, localized renal masses 4 cm or less. Patients without available pre-operative imaging (n= 89, 8%) were excluded from analysis, leaving 1009 to form the study cohort.

2.2 Analysis

The primary end points of this study were (1) the proportion of cases with RCC and (2) the proportion of cases with unfavorable pathologic features at PN. Unfavorable pathology was defined as an RCC with any of the following features: any Fuhrman grade III-IV RCC or lesions upstaged to pathologic T3a. Histological subtype, Fuhrman grade and American Joint Committee on Cancer, Edition 7 stage were recorded for each tumor by an institutional genitourinary pathologist [12]. There was no central pathology review.

Two logistic regression models were created: the first model assessed the probability that an SRM was found to be cancer after PN, and the second model assessed the probability that an SRM was found to harbor unfavorable pathology after PN. Clinical and radiographic characteristics with known associations with the risk of malignancy and unfavorable pathology were chosen for the logistic regression models – notably age [13], sex [13], imaging tumor size [3, 13, 14] and tumor complexity as represented by the R.E.N.A.L. nephrometry score [9, 14, 15].

Univariate and multivariable analyses were performed to determine clinical factors associated with the odds of malignancy and unfavorable pathology. Dichotomous cut points for each continuous variable of interest were determined using the minimum p-value method [16]. A priori cut points of 6, 7 and 8 points for nephrometry score and 2 cm and 3 cm were chosen for size, as these whole number are clinically meaningful. Bootstrap resampling with 500 iterations was performed for each dichotomous cut point to calculate corrected confidence intervals [17]. Discrimination and calibration of the bootstrap adjusted models were analyzed with concordance index and Hosmer-Lemeshow goodness-of-fit test, respectively.

Predictive risk tables for malignancy and unfavorable pathology were constructed from each multivariate model and stratified by the most predictive dichotomous variables.

3. Results

A total of 1009 tumors were identified. Final pathology revealed RCC in 771 (76.3%) and unfavorable pathology in 198 (19.6% of the entire cohort, 25.7% with RCC). Table 1 lists the clinicopathologic characteristics of the cohort.

On univariate analysis, sex, tumor size as a continuous variable and nephrometry sum as a continuous variable were associated both malignancy and unfavorable pathology (Table 2). Neither age nor institution were predictive in either model. Of the a priori cut points evaluated, the cut points with the lowest significant p-value were tumor size of 3 cm and nephrometry sum of 8 points both for prediction of malignancy and unfavorable pathology. On multivariable analysis, male sex, tumor diameter greater or equal to 3 cm and nephrometry sum greater or equal to 8 points were independently predictive of both malignancy and unfavorable pathology (Table 3).

Both models had moderate discrimination ability as measured by the *c* statistic, with 0.62 for the malignancy model and 0.63 for the unfavorable pathology model (Figures 1-2).

Similarly, both models had excellent calibration as measured by the Hosmer-Lemeshow test, with a p value of 0.470 for the RCC model and 0.639 for the unfavorable pathology model, demonstrating no difference between expected and observed event rates (Figure 3-4) [18].

As odds ratios were similar, a risk score was generated by assigning 1 point each for male sex, tumor size > 3 cm and nephrometry sum > 8. The risk score was highly predictive in both the cancer and unfavorable pathology models. Compared to patients with a score of 0, the odds of malignancy increased with each point: 1 point, OR 2.03, 95% CI 1.4-2.92, $p < 0.0001$; 2 points, OR 2.89, 95% CI 1.90-4.40, $p < 0.0001$; 3 points, 4.50, 95% CI 2.19-9.28, $p < 0.0001$. Similarly the odds of unfavorable pathology increased with each point: 1 point, OR 2.43, 95% CI 1.39-4.22, p value = 0.002; 2 points, OR 3.77, 2.14-6.63, $p < 0.0001$; 3 points, OR 5.29, 95% CI 2.70-10.35, $p < 0.0001$). Table 4 shows the full risk score analysis.

Risk tables stratifying by sex, tumor size < or > 3 cm, and nephrometry sum < or > 8 points demonstrated discrimination for both models, as shown in table 5 and 6. Compared to the overall risk of malignancy of the 76.7%, for the entire cohort, patients in the lowest risk stratum (females with tumors < 3 cm and nephrometry sum < 8, or a risk score of 0) had risk of malignancy of 64% (95% CI 58.1-69.7), while patients in the highest stratum (males with tumors > 3 cm and nephrometry sum > 8, or a risk score of 3) who had an 89% (95% CI 85.1 – 92.8) chance of malignancy. Likewise, while the proportion of unfavorable pathology for the entire cohort was 21.8%, patients in the lowest risk stratum had a 9.6% (95% CI 6.6 – 12.6) of unfavorable pathology compared to 35.2% (95% CI 27.8 – 42.7) in the highest stratum.

4. Discussion

Given the biological heterogeneity of SRMs, we embarked to develop risk-stratification tables to better inform patients of their risk of RCC and unfavorable pathology. Using a large, multi-institutional database of over 1,000 patients undergoing extirpative surgery, we found benign pathology in 24% and unfavorable RCC in 20%. Male sex, tumor size and nephrometry score were the strongest predictors of RCC and unfavorable pathology in regression modeling.

Previous attempts at pre-operative risk stratification have assessed both oncologic outcomes and pathologic outcomes in an attempt to characterize the biologic potential of renal masses. Cindolo et al proposed a model predicating recurrence-free survival based on presentation and clinical size [10]. In that series, the mean tumor size was 6.8 cm. Similarly, a European, multi-institutional nomogram used several variables to construct a nomogram with 80% accuracy on external validation [11]. In that study, the mean tumor size was 6.6 cm. Neither study performed subset analyses to analyze the performance of the nomogram in the SRM population, so the validity of those data in the SRM remains unknown.

Frank et al reported the results of 2935 tumors treated at the Mayo Clinic and found that increasing size correlated with higher risk of malignancy, clear cell histology and high Fuhrman grade [3]. The majority of tumors (67%) in that series were 4 cm or greater and 36% were 7 cm or greater. Lane et al developed a nomogram from patients with 7 cm or less

tumors undergoing PN to predict malignancy and potentially aggressive cancers and found that age, sex, tumor size and smoking history were predictive of malignancy and potentially aggressive pathology [8]. In contrast, our study did not demonstrate a relationship with age and either outcome, which may be attributable to the relatively young age of our cohort

A separate predictive tool for tumors ≥ 4 cm is necessary for several reasons. First, there are no existing tools that specifically address the dilemma of the SRM. Secondly, there is little clinical utility in using a nomogram for a large tumor that has a high likelihood of harboring malignancy if it is not going to change management. For example, a patient with a 10 cm renal mass will undergo extirpative surgery if he or she is a surgical candidate. However, predictive tools that include these patients may overestimate the effect of tumor size for patients with smaller tumors. Finally, the relationship between tumor size and biologic potential may not be linear across all tumor sizes. For example, while Karakiewicz et al reported a hazard ratio of 1.19 for cancer-specific survival per cm of tumor size, this relationship may not be constant for all tumor sizes represented in the dataset [11]. Limiting analysis to tumors less than 4 cm reports a clearer picture of the influence of size and its interaction with other variables of interest.

In addition to size, the other variables used in these risk tables have all been confirmed to have predictive significance in previous reports. The influence of gender is well-known.[19] Snyder et al. demonstrated that sex was the only clinical variable associated with benign lesions in a series from Memorial Sloan Kettering.[20] Interestingly, tumor diameter was not predictive of benign pathology in that series. Nephrometry score was first proposed by Kutikov and Uzzo as a way to standardized tumor complexity [21]. It subsequently was used to construct a predictive nomogram along with sex and age that performed well, though with a median tumor size of 4 cm and the inclusion of tumors as large as 25 cm, the interaction of tumor complexity and size among SRM again is unclear. In contrast, Mullins et al found that increasing nephrometry score was a predictor of malignancy but not high grade disease among SRMs [15]. Similarly, multiple studies have demonstrated tumor location is correlated with biologic potentiation, with exophytic tumors exhibiting less malignant lesions and less clear cell histology.[22, 23] Together these studies along with the present study suggest that increasing anatomic complexity is associated with more aggressive biologic potential.

In this study, we report the combination of nephrometry score, tumor size and sex as predictors of cancer and unfavorable pathology. The use of risk tables, rather than a traditional nomogram, may be a less cumbersome tool to use in clinic, is familiar to urologists for the treatment of prostate cancer [24] and is also intuitive for patients to understand. We recognize that the availability of web-based nomograms simplify their use and remain an attractive and powerful alternative.

Traditionally, the treatment paradigm for all SRMs had been surgical extirpation. Because of concerns for over treatment, some proponents of pre-operative biopsy have instead suggested that all patients undergo biopsy prior to surgery [25]. Both of these one-size-fits-all approaches discount the information that can be gleaned from clinical and radiologic risk stratification. In this study, risk stratification based on 3 variables showed that the highest

risk group had an almost 90% of chance of malignancy. Perhaps this is the patient that would not need to undergo renal biopsy. Conversely, a patient with only a 62% chance of malignancy in the lowest risk strata may benefit from improved risk stratification, by biopsy or others means. A risk-stratification scheme based on both clinical information and selective RMB may maximize prognostic information before intervention.

This study has several limitations that warrant discussion. Foremost, the discrimination of this model, is only moderate, albeit comparable in magnitude to other published nomograms [8, 26]. This is likely a reflection of the limit that clinical information alone can offer for this disease. However, knowing the ‘ceiling’ that clinical features alone can offer is necessary to understand the magnitude of prognostic effect that future novel biomarkers may have for SRMs when they are combined with clinical information. It is likely that including tumor size > 4 cm would result in improved discrimination as the proportion of RCC and high-grade tumors rises with increasing size. Another limitation is that design of this multi-institutional registry does not include every possible variable of interest, including risk factors such as smoking status or clinical presentation, or the individual components of the R.E.N.A.L. nephrometry score. It may be possible that these other variables or the components of the nephrometry score could add to the discriminatory power of this model. Additionally, there is no validation cohort to which the risk tables can be applied, although the bootstrap correction does help to address this limitation. We aim to validate these criteria with additional patients as we enroll more patients in our registry. Finally, this registry of patients undergoing robotic PN is subject to selection bias. Surgeon selection of a PN candidate is likely based tumor location and complexity, and it is possible that tumors with higher anatomic complexity and nephrometry score were relegated to a radical nephrectomy. Likewise the median age of this cohort at 59.5 is younger than other series and may limit generalizability to older patients who may be candidates for active surveillance.

Strengths of the study include the large sample size and the inclusion of multiple geographically disparate institutions from which the cohort is formed. Validation of these risk tables in other populations are needed to confirm or adjust their predictive performance.

5. Conclusions

Male sex, tumors size > 3 and R.E.N.A.L. nephrometry score > 8 are predictive of RCC and unfavorable pathology at the time of PN. Although further study is required, risk tables based on these three variables may be useful for pre-operative risk stratification and informed decision making. Novel biomarkers may improve the prognostic accuracy of these models.

Acknowledgments

Funding source: NIH P30CA006973; Buerger Family Scholar Fund

References

- [1]. Nguyen MM, Gill IS, Ellison LM. The evolving presentation of renal carcinoma in the United States: trends from the Surveillance, Epidemiology, and End Results program. *J Urol.* 2006; 176:2397–400. discussion 400. [PubMed: 17085111]

- [2]. Hollingsworth JM, Miller DC, Daignault S, Hollenbeck BK. Rising incidence of small renal masses: a need to reassess treatment effect. *J Natl Cancer Inst.* 2006; 98:1331–4. [PubMed: 16985252]
- [3]. Frank I, Blute ML, Cheville JC, Lohse CM, Weaver AL, Zincke H. Solid renal tumors: an analysis of pathological features related to tumor size. *J Urol.* 2003; 170:2217–20. [PubMed: 14634382]
- [4]. Lane BR, Samplaski MK, Herts BR, Zhou M, Novick AC, Campbell SC. Renal mass biopsy--a renaissance? *J Urol.* 2008; 179:20–7. [PubMed: 17997455]
- [5]. Volpe A, Kachura JR, Geddie WR, Evans AJ, Gharajeh A, Saravanan A, et al. 2007; 178:379–86.
- [6]. Volpe A, Finelli A, Gill IS, Jewett MA, Martignoni G, Polascik TJ, et al. Rationale for percutaneous biopsy and histologic characterisation of renal tumours. *Eur Urol.* 2012; 62:491–504. [PubMed: 22633318]
- [7]. Ball MW, Bezerra SM, Gorin MA, Cowan M, Pavlovich CP, Pierorazio PM, et al. Grade Heterogeneity in Small Renal Masses: Potential Implications for Renal Mass Biopsy. *J Urol.* 2014
- [8]. Lane BR, Babineau D, Kattan MW, Novick AC, Gill IS, Zhou M, et al. A preoperative prognostic nomogram for solid enhancing renal tumors 7 cm or less amenable to partial nephrectomy. *J Urol.* 2007; 178:429–34. [PubMed: 17561141]
- [9]. Kutikov A, Smaildone MC, Eggleston BL, Manley BJ, Canter DJ, Simhan J, et al. Anatomic Features of Enhancing Renal Masses Predict Malignant and High-Grade Pathology: A Preoperative Nomogram Using the RENAL Nephrometry Score. *Eur Urol.* 2011; 60:241–8. [PubMed: 21458155]
- [10]. Cindolo L, de la Taille A, Messina G, Romis L, Abbou CC, Altieri V, et al. A preoperative clinical prognostic model for non-metastatic renal cell carcinoma. *BJU Int.* 2003; 92:901–5. [PubMed: 14632843]
- [11]. Karakiewicz PI, Suardi N, Capitanio U, Jeldres C, Ficarra V, Cindolo L, et al. A preoperative prognostic model for patients treated with nephrectomy for renal cell carcinoma. *Eur Urol.* 2009; 55:287–95. [PubMed: 18715700]
- [12]. Edge, S.; Byrd, D.; Compton, C.; Fritz, A.; Greene, F.; Trotti, A. *AJCC Cancer Staging Manual.* 7th. Springer; New York, New York: 2010.
- [13]. Thompson RH, Kurta JM, Kaag M, Tickoo SK, Kundu S, Katz D, et al. Tumor size is associated with malignant potential in renal cell carcinoma cases. *J Urol.* 2009; 181:2033–6. [PubMed: 19286217]
- [14]. Gorin MA, Ball MW, Pierorazio PM, Tanagho YS, Bhayani SB, Kaouk JH, et al. Outcomes and predictors of clinical T1 to pathological T3a tumor up-staging after robotic partial nephrectomy: a multi-institutional analysis. *J Urol.* 2013; 190:1907–11. [PubMed: 23764083]
- [15]. Mullins JK, Kaouk JH, Bhayani S, Rogers CG, Stifelman MD, Pierorazio PM, et al. Tumor complexity predicts malignant disease for small renal masses. *J Urol.* 2012; 188:2072–6. [PubMed: 23083863]
- [16]. Altman DG, Lausen B, Sauerbrei W, Schumacher M. Dangers of using ‘optimal’ cutpoints in the evaluation of prognostic factors. *J Natl Cancer Inst.* 1994; 86:829–35. [PubMed: 8182763]
- [17]. Holländer N, Sauerbrei W, Schumacher M. Confidence intervals for the effect of a prognostic factor after selection of an ‘optimal’ cutpoint. *Statistics in medicine.* 2004; 23:1701–13. [PubMed: 15160403]
- [18]. Iasonos A, Schrag D, Raj GV, Panageas KS. How to build and interpret a nomogram for cancer prognosis. *J Clin Oncol.* 2008; 26:1364–70. [PubMed: 18323559]
- [19]. Pierorazio PM, Murphy AM, Benson MC, McKiernan JM. Gender discrepancies in the diagnosis of renal cortical tumors. *World J Urol.* 2007; 25:81–5. [PubMed: 17066264]
- [20]. Snyder ME, Bach A, Kattan MW, Raj GV, Reuter VE, Russo P. Incidence of benign lesions for clinically localized renal masses smaller than 7 cm in radiological diameter: Influence of sex. *J Urol.* 2006; 176:2391–5. [PubMed: 17085108]
- [21]. Kutikov A, Uzzo RG. The R.E.N.A.L. nephrometry score: a comprehensive standardized system for quantitating renal tumor size, location and depth. *J Urol.* 2009; 182:844–53. [PubMed: 19616235]

- [22]. Schachter LR, Bach AM, Snyder ME, Kattan MW, Russo P. The impact of tumour location on the histological subtype of renal cortical tumours. *BJU international*. 2006; 98:63–6. [PubMed: 16831144]
- [23]. Venkatesh R, Weld K, Ames CD, Figenshau SR, Sundaram CP, Andriole GL, et al. Laparoscopic partial nephrectomy for renal masses: effect of tumor location. *Urology*. 2006; 67:1169–74. [PubMed: 16765174]
- [24]. Eifler JB, Feng Z, Lin BM, Partin MT, Humphreys EB, Han M, et al. An updated prostate cancer staging nomogram (Partin tables) based on cases from 2006 to 2011. *BJU Int*. 2013; 111:22–9. [PubMed: 22834909]
- [25]. Ordon M, Landman J. Renal Mass Biopsy: "Just Do It". *J Urol*. 2013; 190:1638–40. [PubMed: 23954249]
- [26]. Antonelli A, Furlan M, Sandri M, Minervini A, Cindolo L, Parma P, et al. The RENAL Nephrometric Nomogram Cannot Accurately Predict Malignancy or Aggressiveness of Small Renal Masses Amenable to Partial Nephrectomy. *Clinical genitourinary cancer*. 2014

Figure 1.
Discrimination Plot for RCC Predictive Model

Figure 2.
Discrimination Plot for Unfavorable Pathology Predictive Model

Figure 3.
Calibration Plot for RCC Predictive Model

Figure 4.
Calibration Plot for Unfavorable Pathology Model.

Table 1

Clinicopathologic characteristics of patients with clinical T1a treated with PN

Median age (range)	59.5 (52-67)
Men (%)	607 (60.1)
Imaging tumor diameter	
Median (IQR)	2.4 (1.8-3.0)
No. < 3 cm (%)	717 (71.1)
No. >3 cm (%)	292 (28.9)
Pathologic tumor diameter (IQR)	2.2 (1.6-3.0)
No. RCC (%)	771 (76.3)
Clear Cell	472 (61.9)
Papillary	175 (23.0)
Chromophobe	68 (8.9)
Other	56 (6.2)
Pathologic T Stage (%)	
pT1a	714 (92.6)
pT1b	28 (3.6)
pT3a	29 (3.8)
Fuhrman Grade	
1 – 2	501 (65.0)
3 – 4	188 (24.35)
No Grade *	82 (10.6)
Unfavorable pathology (%) †	198 (19.6)
Grade 3-4 only	169
pT3a only	10
Both grade 3-4 & pT3a	19

* Chromophobe renal cell carcinomas is not routinely graded.

Table 2

Univariate analysis of predictors of malignancy and unfavorable pathology for small renal masses

	Malignancy		Unfavorable Pathology	
	OR (95% CI)	P value	OR (95% CI)	P value
Size, cm(continuous)	1.43 (1.19-1.72)	< 0.0001	1.46 (1.20-1.77)	< 0.0001
Size (categorical)				
< 3 cm	Reference		Reference	
> 3 cm	1.56 (1.11-2.20)	0.004	1.57 (1.13-2.19)	0.003
Nephrometry Sum (continuous)	1.15 (1.06-1.25)	< 0.0001	1.11 (1.02-1.21)	0.011
Nephrometry sum (categorical)				
< 8 points	Reference		Reference	
> 8 points	1.71 (1.24-2.37)	0.001	1.55 (1.13-2.12)	0.007
Sex				
Female	Reference		Reference	
Male	1.94 (1.45 – 2.61)	< 0.0001	2.42 (1.73-3.39)	<0.0001
Age, years (continuous)	.99 (0.98-1.01)	0.26	1.01 (0.99 – 1.02)	0.16
Institution	1.00 (0.91 -1.10)	0.970	1.03 (0.93-1.14)	0.571

Table 3

Multivariable analysis of predictors of malignancy and unfavorable pathology for small renal masses with bootstrap generated 95% confidence intervals

	Malignancy		Unfavorable Pathology	
	OR (95% CI)	P value	OR (95% CI)	P value
Size (categorical)				
< 3 cm	Reference		Reference	
> 3 cm	1.46 (1.02 – 2.11)	0.040	1.46 (1.06-2.02)	0.021
Nephrometry sum (categorical)				
< 8 points	Reference		Reference	
> 8 points	1.64 (1.16 – 2.33)	0.005	1.49 (1.08-2.06)	0.015
Sex				
Female	Reference		Reference	
Male	1.88 (1.39 – 2.55)	< 0.0001	2.35 (1.66-3.32)	< 0.0001

Table 4

Risk Score of predictors of malignancy and unfavorable pathology for small renal masses with bootstrap generated 95% confidence intervals

	Malignancy		Unfavorable Pathology	
	OR (95% CI)	P value	OR (95% CI)	P value
0 points	Reference		Reference	
1 point	2.03 (1.41 – 2.92)	< 0.0001	2.43 (1.39-4.22)	0.002
2 points	2.89 (1.90-4.40)	< 0.0001	3.77 (2.14-6.63)	< 0.0001
3 points	4.50 (2.19-9.28)	< 0.0001	5.29 (2.70-10.35)	< 0.0001

1 pt each for male sex, size > 3 cm, nephrometry sum > 8

Table 5

Predicted Risk of RCC and 95% confidence intervals after PN by sex, size, and nephrometry score

Female		
	Nephrometry < 8	Nephrometry ≥ 8
Size < 3 cm	64.0 (58.1 – 69.7)	74.5 (68.2 – 80.7)
Size ≥ 3 cm	72.2 (64.6 – 79.8)	81.0 (75.0 – 87.1)
Male		
	Nephrometry < 8	Nephrometry ≥ 8
Size < 3 cm	77.0 (72.8 – 81.2)	84.6 (80.3 – 89.0)
Size ≥ 3 cm	83.1 (77.9 – 88.2)	89.0 (85.1 – 92.8)

Value are listed as risk estimated percentage (95% confidence interval)

Table 6

Predicted Risk of Unfavorable pathology and 95% confidence intervals after PN by sex, size, and nephrometry score

Female		
	Nephrometry < 8	Nephrometry ≥ 8
Size < 3 cm	9.6 (6.6 – 12.6)	13.7 (8.2 – 18.1)
Size ≥ 3 cm	13.4 (8.6 – 18.3)	18.8 (12.7 – 24.9)
Male		
	Nephrometry < 8	Nephrometry ≥ 8
Size < 3 cm	20.0 (16.0 – 23.9)	27.1 (21.1 – 33.1)
Size ≥ 3 cm	26.7 (20.2 – 33.2)	35.2 (27.8 – 42.7)

Value are listed as risk estimated percentage (95% confidence interval)