Association between R.E.N.A.L. nephrometry score and perioperative outcomes following open partial nephrectomy under cold ischemia

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Cite as: *Can Urol Assoc J* 2014;8(3-4):e137-41. http://dx.doi.org/10.5489/cuaj.1372
Published online March 11, 2014.

Abstract

Introduction: We investigate the clinical significance of the R.E.N.A.L. nephrometry score for renal neoplasm following open partial nephrectomy (PN) under cold ischemia.

Methods: A retrospective analysis was conducted using clinical data of 98 consecutive patients with clear cell renal cell carcinoma who underwent open PN by a single surgeon from December 2000 to September 2012. Tumour complexity was stratified into 3 categories: low (4-6), moderate (7-9) and high (10-12) complexity. Perioperative outcomes, such as complications, cold ischemic time, estimated blood loss and renal function, were analyzed according to the complexity by NS. Complications were stratified using the Clavien-Dindo classification system.

Results: Tumour complexity according to nephrometry score was assessed as low in 16 (16.3%), moderate in 48 (49.0%) and high in 34 (34.7%). The median cold ischemic time did not differ significantly among the 3 groups (36.0 minutes in low-, 40 minutes in moderate- and 43 minutes in the high-complexity group, $p = 0.421$). Total complications did not differ significantly (2 (2.0%) in low, 4 (4.1%) in moderate and 4 (4.1%) in high, $p = 0.984$). Each Grade 3 complication occurred in the moderate (urine leakage) and high groups (lymphocele). Postoperative renal functional outcomes were similar among the groups ($p = 0.729$). Only mean estimated blood loss was significantly different with nephrometry score ($p = 0.049$).

Conclusions: The nephrometry score, as used in an open PN series under cold ischemia, was not significantly associated with perioperative outcomes (i.e., ischemia time, complications, renal functional preservation).

Introduction

Detection and management of renal tumours are common for practicing urologists.[1,2] The traditional standard of care is radical nephrectomy for a renal tumour. However, as new technologies and advanced imaging procedures develop, partial nephrectomy (PN) has become popular surgery for extracting renal tumours. PN has demonstrated oncological outcomes similar to radical nephrectomy with benefits in overall survival likely secondary to preservation of renal function.[3,4]

To better facilitate inter-physician communication and allow for more accurate case series comparisons in the literature, Kutikov and Uzzo devised the R.E.N.A.L. nephrometry scoring system.[5] This scoring system has been proposed to characterize a renal tumour based on tumour radius, endophyticity level, nearness to collecting system,and location (R.E.N.A.L.). The R.E.N.A.L nephrometry score was developed based on what the authors believed were characteristics that rendered tumours more difficult to achieve PN.[6] Since its introduction, the R.E.N.A.L. nephrometry score has shown its prognostic capability with respect to postoperative outcomes, such as reducing warm ischemic time and reducing surgery-related complications.[7,8] However, there is some debate on whether it can predict renal functional outcomes and surgery-related outcomes.[6,9-11] Moreover, these studies mostly applied to the patients who underwent robotic partial nephrectomy (RPN) or laparoscopic partial nephrectomy (LPN), minimally invasive surgeries that used warm ischemia methods. In this study, we applied the nephrometry score to patients who underwent open partial nephrectomy (OPN) with cold ischemia and we confirm the usefulness of the nephrometry score to confirm postoperative outcomes.

Methods

Study population

We consulted our prospectively maintained institutional kidney centre database, after we obtained approval by our Institutional Review Board. We identified all patients from December 2000 to September 2012 who underwent PN with available cross-sectional imaging by computerized tomography (CT) for assessment. We excluded patients who had solitary kidney, chronic kidney insufficiency and previous kidney surgery. We also excluded patients with benign lesions or non-clear cell renal cell carcinoma (RCC). In the end, we included 98 patients who underwent OPN under cold ischemia. The surgical technique for OPN, as previously reported, was used in all patients.[12] The secure reconstruction technique was applied using a combination of expanded polytetrafluoroethylene and Hem-O-Lok (Weck Surgical Instruments, Teleflex Medical, Durham, NC) to reduce surgery-related complications.

Evaluation

Preoperative CT imaging was reviewed in the axial and coronal planes, and a nephrometry score was assigned to all identified lesions, as described by Kutikov and Uzzo.[5] All score assignments were performed by at least 2 investigators with conflicting data reviewed. Each tumour was scored for total nephrometry score and for each of its individual subcategories. The nephrometry score was categorized as low (4-6 points), moderate (7-9 points) or high (10-12 points) complexity. The perioperative outcomes, such as complications, cold ischemic time, estimated blood loss and renal functional outcomes, were analyzed according to the stratification of complexity by nephrometry score. Intra- and postoperative complications were stratified using the Clavien-Dindo classification system.[13]

Statistical analysis

Demographic and clinical characteristics were compared between tumour complexity groups. Continuous variables were analyzed by Wilcoxon tests, and categorical variables were examined by chi-square analyses. Statistical analyses were carried out using SPSS version 15.0 software (Statistical Package for Social Sciences, Chicago, IL). Two-tailed null hypotheses of no difference were rejected if *p* values were less than 0.05.

Results

The mean age of all study subjects was 53.8, the mean tumour size was 3.87 cm and the mean cold ischemic time was 42.5 minutes (Table 1). Patients were followed for a median 47.5 months. There were 16 (16.3%), 48 (49.0%), 34 (34.7%) patients in the low-, moderate- and high-complexity group, respectively. Tumour size was significantly larger by complexity grade: 2.78 cm, 3.55 cm and 4.85 cm in the low-, moderate-, and high-complexity groups, respectively. There were no significant differences with respect to age, gender and body mass index. In terms of operative data, total operation time and cold ischemic time were not significantly different among the case series. The cold ischemic time was 38.8 minutes, 44.1 minutes and 45.4 minutes in the low-, moderate-, and high-complexity groups, respectively. Only estimated blood loss was higher by complexity grade (195 vs. 261 vs. 285 cc, low vs. moderate vs. high, respectively). No radical conversion was reported. All pathological types of tumour among subjects were clear cell RCC: T1a was 84 (85.7%), T1b was 8 (8.2%), T2 was 1 (1.0%) and T3a was 5 (5.1%). Pathological T1b and T2 tumour were significantly included in higher complexity group; however, there was no significant difference of Fuhrman grade according to tumour complexity.

Table 1. Patient demographics and tumour characteristics according to complexity grade

	All patients	Low complexity group	Moderate complexity group	High complexity group	*p* value
Nephrometry score		4-6	7-9	10-12	
N (%)	98	16 (16.3)	48 (49.0)	34 (34.7)	
Age, year ± SD	53.8 ± 12.6	59.6 ± 11.3	53.7 ± 11.8	51.1 ± 13.8	0.084
Gender, n (%)					0.784
Male	58 (59.2)	13 (81.3)	29 (60.4)	16 (47.1)	
Female	40 (40.8)	3 (18.7)	19 (39.6)	18 (52.9)	
BMI, kg/m^2 ± SD	24.4 ± 2.4	24.2 ± 2.6	24.4 ± 2.2	24.6 ± 2.8	0.164
Preoperative tumour size (cm)	3.87 ± 3.17	2.78 ± 1.42	3.55 ± 1.40	4.85 ± 4.93	0.006
Median follow-up, months	47.5 ± 11.3	53.6 ± 7.8	44.5 ± 3.8	48.6 ± 12.3	0.881
Operative data					
Estimated blood loss, mL	263.7 ± 140.1	195.0 ± 74.1	261.1 ± 87.1	285.1 ± 110.3	0.049
Ischemic time, min	42.5 ± 15.6	36.3 ± 15.9	40.1 ± 12.6	43.4 ± 11.3	0.421
Operative time, min	183 ± 13.4	167 ± 23.8	180.1 ± 22.3	178.5 ± 37.9	0.191
Pathologic stage (T1a/T1b/T2/T3a)	84/8/1/5	15/0/0/1	45/2/0/2	24/6/1/2	0.037
Furhman grade (1/2/3/4)	4/50/38/6	1/9/6/0	1/25/19/3	2/16/13/3	0.500
Positive surgical margin, (%)	2 (2.0)	0	1 (1.0)	1 (1.0)	0.781

SD: standard deviation; BMI: body mass index.

Among the 98 patients, there were 11 complications (Table 2). Two (2.0%) were in the low complexity group, and 4 (3.1%) in the moderate and high complexity groups. Nine complications were Clavien-Dindo classification I and II; there were only 2 ≥3 grade complications. In the low complexity group, all 2 complications were wound cellulitis. In the moderate complexity group, there were 4 complications: 1 persistent hematuria, 1 wound cellulitis, 2 bleeding requiring transfusion and 1 lymphocele requiring percutaneous drainage under interventional therapy. In the high complexity group, there were also 4 complications: 1 persistent hematuria, 2 bleeding requiring transfusion and 1 urinary leakage requiring ureteral stent insertion. There were no significant differences in terms of complications by tumour complexity grade.

Table 3 presents postoperative renal functional outcomes. There was no significant difference of preoperative estimated glomerular filtration rate (eGFR) or serum creatinine. After OPN, postoperative eGFR and serum creatinine were similar at 1 month and 6 months. The change of eGFR and serum creatinine was also similar among the case series.

Discussion

In the current study, we observed that nephrometry score applied to OPN series under cold ischemia was not significantly associated with perioperative outcomes, especially ischemic time, complications and postoperative renal functional preservation among a consecutive case series of Korean men.

Advanced image techniques have led to a marked increase in the number of incidentally discovered small renal masses.[14] Migration of stage has allowed less invasive surgery, including LPN. PN has equivalent disease-specific outcomes compared with RN, with improved renal functional outcomes.[15,16] Unfortunately, LPN is considerably more challenging, with parameters that predict surgical difficulty before the actual surgery. Therefore, nephrometry score might be introduced in the era of LPN because the PN surgical approach does not effectively reduce ischemic time.

Several previous studies of the correlation of nephrometry score with ischemic time showed mostly positive associations, especially from LPN or RPN case series. Hayn and colleagues concluded that a higher nephrometry score was significantly associated with an increased warm ischemic time in their LPN case series.[17] In their RPN series, Png and colleagues showed that complex tumours with a higher nephrometry scores had significantly high ischemic times compared with non-complex tumours.[11] In their minimally invasive PN case series, Liu and colleagues[18] and Altunrende and colleagues[9] found that nephrometry score was predictive of warm ischemic time, and mean warm ischemic time increased significantly by tumour complexity. Some data from OPN series also showed positive correlation of nephrometry score with warm ischemic time. Long and colleagues found that among patients who mostly under-

Table 2. Perioperative complications according to complexity grade

	Low complexity group	Moderate complexity group	High complexity group	*p* value
Nephrometry score	4–6	7–9	10–12	
N (%)	16 (16.3)	48 (49.0)	34 (34.7)	
No. complications (%)	2 (2.0%)	4 (4.1%)	4 (4.1%)	0.984
Clavien-Dindo class I				
Persistent hematuria	0	1 (1.0%)	1 (1.0%)	0.874
Wound cellulitis	2 (2.0%)	1 (1.0%)	0	0.474
Clavien-Dindo class II				
Bleeding requiring transfusion	0	2 (2.0%)	2 (2.0%)	0.678
Clavien-Dindo class III-VI				
Urine leakage	0	0	1 (1.0%)	0.477
Lymphocele	0	1 (1.0%)	0	0.674

Table 3. Postoperative renal functional outcome after open partial nephrectomy according to tumour complexity

	Low complexity group	Moderate complexity group	High complexity group	*p* value
Nephrometry score	4–6	7–9	10–12	
Mean ± SD				
Preoperative eGFR	72.2 ± 25.3	72.9 ± 19.9	77.9 ± 25.3	0.592
Preoperative Cr	1.04 ± 0.26	1.02 ± 0.22	1.03 ± 0.55	0.982
Postoperative 1 month eGFR	72.6 ± 27.6	72.6 ± 18.1	77.9 ± 26.9	0.588
Postoperative 1 month Cr	1.05 ± 0.26	1.02 ± 0.24	1.01 ± 0.49	0.951
Change in eGFR at 1 month	0.40	-0.30	0	0.974
Postoperative 6 months eGFR	67.5 ± 23.5	72.8 ± 20.3	70.1 ± 23.2	0.729
Postoperative 6 months Cr	1.07 ± 0.33	1.04 ± 0.24	1.13 ± 0.54	0.726
Change in eGFR at 6 months	-4.7	-0.10	-7.8	0.367

eGFR: estimated glomerular filtration rate (mL/min/1.73m^2), Cr: creatinine (mg/dL).

went OPN, the nephrometry score predicted increased risk of prolonged warm ischemic time.[10] In their OPN series, Lavallee and colleagues found that several parameters of tumour complexity positive correlated with warm ischemic time.[19] However, Mufarrij and colleagues demonstrated that nephrometry-graded tumour complexity was not related to warm ischemic time for 92 patients who underwent RPN.[20] Their interpretation was that since their series was based on the skills of a highly experienced laparoscopic and robotic surgeons, differences between simple and complex cases were too minuscule to detect. They also cited several selection biases. Our analysis was the first report of the correlation of nephrometry score with ischemic time in OPN under cold ischemia. In cold ischemia, there is little time pressure compared with warm ischemia. In a PN series, ischemic time is usually accepted as the parameter for evaluating operative outcomes, 30 minutes or less has historically been used as the warm ischemic time.[21] More recently, other studies proposed a 20-minute cut-off.[22,23] Because of this tight time limit in PN and the need to speed up the procedure, there were several complications. Recent studies showed that most PN used warm ischemia. As laparoscopic and robotic PN procedures were introduced, warm ischemia was standard practice worldwide (and even applied in OPN). The range of safe warm ischemic time should be less than 20 or 30 minutes for controlling postoperative renal function or complications.[22.23] Although renal functional preservation should be based on normal function of the contralateral kidney, actual postoperative renal function after PN was assessed by renal functional volumetric change.[2] Because the nephrometry score had a factor of tumoural volume representing tumoural diameter, some reports in which higher nephrometry score was associated with poorer renal functional outcome following PN had adequate evidence.[24] If the same renal functional volume is lost, we should use cold ischemia in PN. In situ renal hypothermia is used to protect against ischemic renal injury. Surface cooling of the kidney with ice slush allows up to 3 hours of safe ischemia without permanent renal injury.[25,26] Therefore our analysis from PN case series using cold ischemic type showed no significant difference of ischemic time according to nephrometry score grade, because there was no real time pressure even with a large-sized tumour.

Concerning complications, there were controversial conclusions. Stroup and colleagues showed that nephrometry score was associated with urine leak in the Mayo clinic database.[27] Rosevear and colleagues concluded that nephrometry score was a significant predicting factor for complication after PN among 91 patients. Simhan and colleagues also showed that increases of renal complexity were associated with the development of major complications after PN among 390 consecutive patients.[28] However, Long and colleagues[10] confirmed the link between nephrometry score and complication risk; there was no significant correlation of nephrometry score with complication risk among the mainly OPN series. In their RPN series, Png and colleagues showed similar complication rates between complex and non-complex tumours. In our results, we observed no significant difference among nephrometry scores. We found that by using cold ischemia, we had spare time during surgery to allow for more delicate procedures, such as renal reconstruction or repair of the collecting system. Especially in our series, we were able to use secure reconstruction techniques using Gore-Tex and Hem-o-Lok (Dupont).[12] This may have led to the low complication rate in the total case series, and no significant differences according to nephrometry score grade.

Our study had several limitations. We had a sample number disparity according to nephrometry score; only 16.3% of 98 patients were included in the low complexity tumour grade. This data from our kidney centre database were consecutive data, so further study is needed to adjust for sample size in each NS group. Another limitation was the relatively low total complication rate. Although more secure techniques were performed in all patients, there was the possibility of false negative effects due to relatively small cohort. Another limitation was that we could not adjust contralateral kidney function. If we had known the actual effect of renal function after PN according to tumour complexity, this might be used in a solitary kidney case series or for adjusting contralateral kidney function. However, we could not do this practically. Further evaluation about this topic should be conducted via prospective well-controlled randomized studies, while adjusting for other factors. Another limitation was that we could not control other medical problems or medication history that might affect renal function preoperatively due to the retrospective design. We minimized other limitations by collecting only clear cell RCC data from a single surgeon's database, measuring the nephrometry score for each patient by a single urologist. Further study is needed to estimate the association of tumour complexity with malignancy among all kidney centre databases similar to the study by Mullins and colleagues.[29]

Conclusion

OPN under cold ischemia was safely performed regardless of tumour complexity. Applying nephrometry score to an OPN series under cold ischemia was not significantly associated with perioperative outcomes. The cold ischemia time, complication rate and renal functional outcomes after PN was similar by nephrometry score grade. To minimize complications, renal functional loss and other surgery-related hazards regardless of tumour complexity, PN with cold ischemia is recommended.

Competing interests: Dr. Park, Dr. Hwang, Dr. Kang and Dr. Oh all declare no competing financial or personal interests.

This paper has been peer-reviewed.

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