



Kidney Cancer

Robotic Partial Nephrectomy for Renal Tumors Larger Than 4 cm

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Abstract

Background: Minimally invasive partial nephrectomy (PN) is most commonly performed for renal tumors ≤ 4 cm in size. Robotic PN (RPN) for tumors >4 cm has not been assessed.

Objective: To evaluate the safety and feasibility of RPN for tumors >4 cm in the context of patients undergoing RPN for tumors ≤ 4 cm.

Design, setting, and participants: We reviewed data for 71 consecutive patients who underwent transperitoneal RPN at a tertiary care center between August 2007 and September 2009 by a single surgeon. Patients were stratified into two groups: 15 with tumors >4 cm on preoperative imaging (group 1) and 56 patients with tumors ≤ 4 cm (group 2).

Intervention: All patients underwent transperitoneal RPN by a single surgeon.

Measurements: Preoperative, perioperative, pathologic, and functional outcomes data were analyzed and compared between groups. We used χ^2 and student *t* tests for categorical and continuous variables, respectively. A *p* value <0.05 was considered statistically significant.

Results and limitations: Mean radiographic tumor size was 5.0 cm (4.1–7.9) for group 1 and 2.1 cm (0.7–3.8) for group 2. No significant differences were found between groups for estimated blood loss, total operative time, hospital stay, complication rates, and change in estimated glomerular filtration rate. Patients with larger tumors had longer median warm ischemia times (25 vs 20 min; *p* = 0.011). Limitations of our study include the retrospective nature the analysis, small sample size, and single-surgeon experience.

Conclusions: In our initial experience, RPN for tumors >4 cm is safe and feasible, showing comparable outcomes to RPN for smaller tumors, although with longer warm ischemia times. Future studies with extended follow-up are necessary to determine the viability of RPN for large tumors as an effective form of treatment.

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1. Introduction

Nephron-sparing surgery has become an established approach for small renal tumors, demonstrating equivalent

oncologic efficacy to radical nephrectomy (RN) [1–3] with the advantage of preservation of renal function and possibly improved survival. Laparoscopic partial nephrectomy (LPN) has demonstrated comparable oncologic and functional

outcomes to open partial nephrectomy (OPN) [4]; however, partial nephrectomy (PN) for larger tumors may pose additional technical challenges during surgery. OPN has been described for patients with tumors >4 cm in size with satisfactory results [3]. LPN has also been described for patients with tumors >4 cm [5,6], but technical challenges may be even more pronounced with a laparoscopic approach than with an open approach.

Robotic assistance during PN is a relatively new approach, with a number of studies demonstrating its feasibility and safety for small renal tumors [7–10]. To the best of our knowledge, no studies evaluate robotic PN (RPN) for tumors >4 cm. We evaluate early surgical, functional, and oncologic outcomes of RPN for renal tumors >4 cm on preoperative imaging and compare these results to outcomes for tumors ≤4 cm.

2. Patients and methods

Data for 71 consecutive patients who underwent transperitoneal RPN at our institution between August 2007 and September 2009 by a single surgeon (CGR) were reviewed from a prospectively maintained, institutional review board–approved database. Tumor size was assessed preoperatively with either computed tomography or magnetic resonance imaging. Patients were stratified into two groups based on clinical tumor size: 15 patients with tumors >4 cm (group 1) and 56 patients with tumors ≤4 cm (group 2).

Preoperative demographic factors analyzed included age, gender, surgical side, body mass index, American Society of Anesthesiologists classification, and a history of previous abdominal surgery. The location, endophytic nature, and proximity to the collecting system of the tumor were assessed using preoperative imaging. The number of procedures performed for incidentally discovered masses and imperative indications (solitary kidney, bilateral renal masses, stage 3 or worse chronic kidney disease) was also assessed.

Our RPN technique has been described elsewhere, and a detailed description of technique is beyond the scope of this report [11–13]. Briefly, patients are placed in flank position, and ports are placed as demonstrated in Fig. 1. The da Vinci robot system (Intuitive Surgical, Sunnyvale, CA, USA) is used in all cases. For large or challenging tumors, a four-arm approach is used. The fourth robotic arm can be used for tasks such as providing kidney retraction, placing the kidney on stretch for

dissection of renal vessels, and positioning the kidney for optimal tumor resection.

Bowel mobilization and kidney exposure are performed with complete robotic assistance. The renal hilum is dissected, and the perinephric fat is reflected to expose the capsule and tumor. Laparoscopic ultrasonography is used to confirm tumor location, extent, and depth, with real-time imaging displayed in the viewfinder using TilePro software (Intuitive Surgical, Sunnyvale, CA, USA). The renal capsule is scored to demarcate margins of resection. Hilar occlusion is performed in the majority of cases using either laparoscopic bulldog clamps or a Satinsky clamp.

For large, endophytic, or central tumors, we generally clamp both the artery and the vein. For small, peripheral, cortical tumors, we may clamp the artery alone. Tumor excision is performed sharply with robotic scissors, ensuring adequate surgical margins. Large vessels and collecting system defects are oversewn using 3-0 or 4-0 monocril or polyglactin sutures with a Lapra-Ty (Ethicon, Cincinnati, OH, USA) clip instead of tied knots. In our early experience, the renal capsule was reapproximated using 0 polyglactin sutures anchored with Lapra-Ty clips, transitioning later to Hem-o-lok clips (Teleflex Medical, Research Triangle Park, NC, USA) with the sliding clip renorrhaphy technique. The opposite side is secured by a Hem-o-lok clip that the console surgeon slides down to reapproximate capsular edges under tension [14]. For larger tumors leaving a broad defect, bolsters and thrombogenic agents may be used.

Perioperative factors analyzed included total operative time (including abdominal insufflation, port placement, robot docking, specimen extraction, and closure), warm ischemia time, hilar clamping technique, estimated blood loss (EBL), conversion rate, change in 24-h postoperative hemoglobin, length of hospital stay, and length of follow-up. Complications were recorded using the Clavien classification system [15]. Change in estimated glomerular filtration rate (GFR) from baseline was assessed 24 h postoperatively and at follow-up of 1–3 mo postoperatively using the Modification of Diet in Renal Disease equation [16]. Pathologic factors analyzed included pathologic tumor size, histology, pathologic stage using the 2002 American Joint Committee on Cancer staging criteria, Fuhrman grade, and positive surgical margin (PSM) rate.

Preoperative and perioperative results as well as pathologic and functional outcomes data were retrospectively analyzed and compared between groups. Statistical analysis was performed using Stata v.10 (StataCorp, College Station, TX, USA). Comparisons between groups were performed using χ^2 and student *t* tests for categorical and continuous variables, respectively. A *p* value <0.05 was considered statistically significant.

3. Results

A total of 71 patients underwent transperitoneal RPN at our institution during the study period, of which 15 patients had tumors >4 cm on preoperative imaging. Baseline demographics and radiographic tumor characteristics are summarized in Table 1. There was no significant difference in baseline characteristics between groups. Mean radiographic size was 5.0 cm (range: 4.1–7.9) and 2.1 cm (range: 0.7–3.8) for groups 1 and 2, respectively (*p* < 0.001).

Perioperative variables are summarized in Table 2. Intraoperative variables, including EBL, clamping technique, and conversion rate, were similar between groups. One patient in group 2 with normal renal function and a normal contralateral kidney was electively converted from RPN to robotic RN because of an intraoperative finding of multifocal, satellite lesions positive for renal cell carcinoma (RCC)

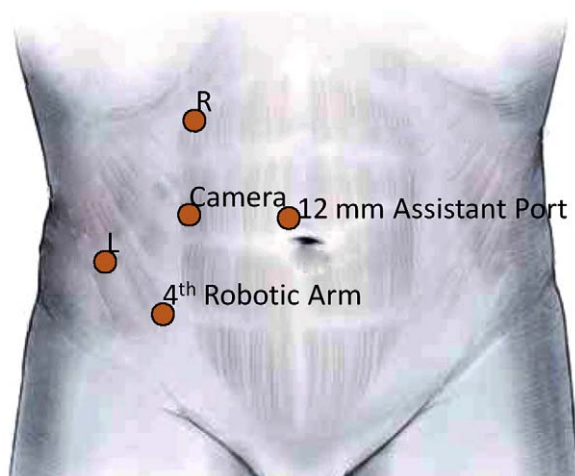


Fig. 1 – Port placement during robotic partial nephrectomy.

Table 1 – Preoperative variables for patients undergoing robotic partial nephrectomy

Characteristic		Group 1 (>4 cm)	Group 2 (≤4 cm)	p value
Patients, no.		15	56	–
Demographic variables				
Mean age, yr (range)		59.0 (44–76)	60.1 (35–81)	0.657
Gender, No. (%)	Male	9 (60)	35 (62.5)	0.859
	Female	6 (40)	21 (37.5)	–
Tumor side, No. (%)	Left	9 (60)	37 (66.1)	0.662
	Right	6 (40)	19 (33.9)	–
Mean BMI, kg/m ² (range)		32.1 (18.4–48.8)	30.6 (20.5–49)	0.726
ASA classification score, No. (%)	1	0 (0)	1 (2.0)	0.852
	2	5 (41.7)	18 (36.7)	–
	3	7 (58.3)	30 (61.2)	–
Previous abdominal surgery, No. (%)	Yes	2 (13.3)	15 (26.8)	0.278
	No	13 (86.6)	41 (73.2)	–
Incidental finding, No. (%)	Yes	11 (73.3)	41 (73.2)	0.993
	No	4 (26.7)	15 (26.8)	–
Imperative indication for PN, No. (%)	Yes	1 (6.6)	7 (12.5)	0.526
	No	14 (93.3)	49 (87.5)	–
Radiographic variables				
Mean tumor size, cm (range)		5.0 (4.1–7.9)	2.1 (0.7–3.8)	<0.001
Tumor location, No. (%)	Upper	7 (46.6)	18 (32.1)	0.427
	Mid	4 (26.6)	25 (44.6)	–
	Lower	4 (26.6)	13 (23.2)	–
Percent endophytic, No. (%)	<50%	11 (84.6)	28 (53.8)	0.115
	50– <100%	2 (15.3)	19 (36.5)	–
	100%	0 (0)	5 (9.6)	–
Abutting collecting system, No. (%)	Yes	10 (71.4)	31 (55.3)	0.275
	No	4 (26.6)	25 (44.6)	–

BMI = body mass index; ASA = American Society of Anesthesiologists; PN = partial nephrectomy.

Table 2 – Perioperative variables for patients undergoing robotic partial nephrectomy

Characteristic		Group 1 (>4 cm)	Group 2 (≤4 cm)	p value
Intraoperative variables				
Median total operative time, min (IQR)		275.5 (229–344)	238 (210–289)	0.068
Median warm ischemia time, min (IQR)		25 (20–30)	20 (14–24.5)	0.011
Median EBL, ml (IQR)		100 (75–200)	100 (50–200)	0.287
Elective conversions, No. (%)		0 (0)	1 (1.8)	0.602
Clamping technique, No. (%)	None	2 (13.3)	12 (21.4)	0.400
	Bulldog	13 (86.6)	40 (71.4)	–
	Satinsky	0 (0)	4 (7.1)	–
Collecting system repair, No. (%)	Yes	10 (71.4)	31 (55.3)	0.275
	No	4 (26.6)	25 (44.6)	–
Postoperative variables				
Median length of stay, d (IQR)		2 (2–4)	2 (2–3)	0.197
Mean change in 24-h hemoglobin, g/dl (range)		–2.4 (–4.5 to –0.9)	–1.7 (–4.0 to 0.7)	0.259
Mean follow-up, mo (range)		7.9 (0.7–25.0)	6.5 (0.3–19.3)	0.286

IQR = interquartile range; EBL = estimated blood loss.

on frozen section and poorly visualized on intraoperative ultrasound. The majority of cases in both groups were performed under warm ischemia (86.6% vs 78.5%; $p = 0.400$). Median warm ischemia time was longer for tumors >4 cm (25 vs 20 min; $p = 0.011$). Median total operative time was also longer for tumors >4 cm (275.5 vs 238 min) but did not reach statistical significance ($p = 0.068$). No patients required an intraoperative blood transfusion. Postoperative factors were similar between groups with regard to hospital stay, change in 24-h postoperative hemoglobin, and follow-up. The overall mean

follow-up for our study was 6.8 mo, with the longest follow-up to date at 25 mo. There has been no disease-specific mortality in our series to date.

A detailed comparison of intraoperative and postoperative complications is summarized in Table 3. Four complications occurred in group 1, including two postoperative urine leaks and two bleeds. Six complications occurred in group 2, including an intraoperative enterotomy (repaired robotically without sequelae), postoperative pneumonia, pulmonary embolism, and bleeding. There was no difference in intraoperative complications

Table 3 – Comparison of intraoperative and postoperative complications

	Group 1 (>4 cm)	Group 2 (≤4 cm)	p value
Intraoperative complication, No. (%)			
No	15 (100)	55 (98.2)	0.602
Yes	0 (0)	1 (1.8)	–
Postoperative complication, No. (%)			
No	11 (73.3)	51 (91.1)	0.067
Yes	4 (26.6)	5 (8.9)	–
Complication			
Intraoperative, No. (%)			
Enterotomy [*]	0 (0)	1 (1.8)	–
Postoperative, No. (%)			
Atelectasis	0 (0)	1 (1.8)	–
Urinary retention	0 (0)	1 (1.8)	–
Urine leak ^{**}	2 (13.2)	0 (0)	–
Bleeding [†]	2 (13.2)	2 (3.6)	–
Pulmonary embolism	0 (0)	1 (1.8)	–
Postoperative complications (Clavien classification), No. (%)			
1	0 (0)	2 (3.6)	0.522
2	1 (6.6)	1 (1.8)	–
3a	2 (13.2)	1 (1.8)	–
3b	0 (0)	0 (0)	–
4a	1 (6.6)	1 (1.8)	–
4b	0 (0)	0 (0)	–
5	0 (0)	0 (0)	–

^{*} Enterotomy during lysis of adhesions; repaired robotically without sequelae.

^{**} Urine leaks resolved spontaneously after stenting.

[†] Bleeding resolved spontaneously after transfusion in one patient in each group. One patient in group 1 with platelet dysfunction required reexploration for delayed rupture of a hepatic subcapsular hematoma. One patient in group 2 had a parenchymal bleed requiring angioembolization.

Table 4 – Change in renal function in patients undergoing robotic partial nephrectomy^{*}

	Group 1 (>4 cm) (n = 9)	Group 2 (≤4 cm) (n = 28)	p value
Mean baseline estimated GFR, No. (range)	86.2 (57.3–168.7)	73.5 (37.5–107.0)	0.447
Mean 24-h postoperative estimated GFR, No. (range)	58.4 (33.3–97.3)	68.9 (37.5–113.4)	0.119
Mean change in 24-h postoperative estimated GFR from baseline, No. (range)	–13.9 (–102.5 to 64.2)	–4.6 (–30.7 to 32.0)	0.295
Mean follow-up estimated GFR (1–3 mo), No. (range)	74.0 (33.3–168.7)	76.5 (27.4–126.9)	0.339
Mean change in follow-up estimated GFR (1–3 mo) from baseline, No. (range)	–12.3 (–64.2 to 28.6)	3.0 (–37.3 to 64.8)	0.063

GFR = glomerular filtration rate.

^{*} Patients were included if they had preoperative, 24-h postoperative, and follow-up creatinine within 1–3 mo of surgery. All values in milliliter per minute per 1.73 m².

between groups ($p = 0.602$). Postoperative complications were higher for tumors >4 cm (26.6% vs 8.9%), although this difference did not reach statistical significance ($p = 0.067$). There was no difference in the severity of complications between groups based on the Clavien classification ($p = 0.522$). Renal function at baseline, postoperatively, and at follow-up is summarized in Table 4. Estimated GFR was higher preoperatively in group 1 (86.2 vs 73.5 ml/min per 1.73 m²; $p = 0.447$) but lower 24 h postoperatively (58.4 vs 68.9 ml/min per 1.73 m²; $p = 0.119$) and at 1–3-mo follow-up (74.0 vs 76.5 ml/min per 1.73 m²; $p = 0.339$), but none of these differences was statistically significant. Mean change in 24-h and 1–3-mo postoperative estimated GFR from baseline were greater for tumors >4 cm, but neither of these changes reached statistical significance ($p = 0.295$ and 0.063, respectively).

Final pathology revealed malignant tumors in 66.6% and 73.2% of patients in groups 1 and 2, respectively. Comparisons of pathologic variables are shown in Table 5. Mean pathologic tumor size was 5.2 cm (range: 3.6–8.1) versus 2.1 cm (range: 0.8–4.2) for groups 1 and 2, respectively ($p < 0.001$). There were three focal microscopic positive surgical margin (PSM) in group 2, of which two patients had undergone enucleation for angiomyolipoma, resulting in an overall PSM rate of 1.96% for malignancy. The patient is undergoing close observation with no evidence of local recurrence at 12-mo follow-up. There were no grossly positive margins.

4. Discussion

PN has demonstrated equivalent cancer control to RN for small renal masses [1,2], with improved long-term clinical,

Table 5 – Pathologic variables for patients undergoing robotic partial nephrectomy

Characteristic		Group 1 (>4 cm)	Group 2 (≤4 cm)	p value
All patients				
Histology, No. (%)	RCC	10 (66.6)	41 (73.2)	0.813
	AML	3 (20)	6 (10.7)	–
	Oncocytoma	1 (6.6)	4 (7.1)	–
	Other benign	1 (6.6)	5 (8.9)	–
Mean pathologic size, cm (range)		5.2 (3.6–8.1)	2.1 (0.8–4.2)	<0.001
PSM, No. (%)		0 (0)	3 (5.3)	0.360
RCC patients				
Subtype, No. (%)	Clear cell	5 (50)	25 (61.0)	0.366
	Papillary	4 (40)	8 (19.5)	–
	Chromophobe	1 (10)	8 (19.5)	–
Fuhrman grade, No. (%)	1	0 (0)	5 (15.6)	0.267
	2	4 (44.4)	17 (53.1)	–
	3	5 (55.5)	10 (31.3)	–
	4	0 (0)	0 (0)	–
Pathologic stage, No. (%)	pT1a	2 (20)	37 (90.2)	<0.001
	pT1b	7 (70)	0 (0)	–
	pT2	0 (0)	0 (0)	–
	pT3a	1 (10)	4 (9.8)	–
Mean pathologic size, cm (range)		5.2 (3.6–8.1)	2.1 (0.8–4.2)	<0.001
PSM, No. (%)		0 (0)	1 (2.4)	0.601

RCC = renal cell carcinoma; AML = angiomyolipoma; PSM = positive surgical margins.

functional, and survival outcomes over RN [17–21]. LPN, which was introduced in 1993 [22,23], has emerged as a viable alternative for the surgical management of small renal masses, with oncologic and functional outcomes similar to OPN [4,24,25]. However, LPN is technically challenging, requiring advanced skills to perform precise tumor excision and intracorporeal sutured reconstruction while minimizing ischemia times. Large tumors may present additional technical challenges during PN that may add to the challenges of LPN. Robotic assistance may help overcome technical challenges of LPN, including tumor resection and renal reconstruction under warm ischemia. A number of studies have demonstrated the feasibility of RPN [7–10,13,26,27].

PN for tumors >4 cm has been described with satisfactory results with an open approach [3–9], and limited reports from experienced surgeons have demonstrated feasibility with a laparoscopic approach [5,6]. Our study is the first to evaluate RPN with a specific focus on patients with tumors >4 cm and to compare outcomes with RPN for tumors ≤4 cm.

Rais-Bahrami et al. [5] compared results of LPN for patients with tumors >4 cm (34 patients) and ≤4 cm (274 patients). There were no differences in preoperative characteristics or intraoperative outcomes between groups. Patients with larger tumors had more complications (32.3 vs 25.1%, $p = 0.039$) and longer hospital stays (4.1 vs 3 d; $p = 0.026$). Simmons et al. [6] compared results of LPN for patients with tumors >4 cm (58 patients) to 2–4 cm (278 patients) and <2 cm (89 patients). There were no differences between groups in operative time, EBL, and hospital stay. Patients with larger tumors were more likely to require pelvic/abdominal repair and had a longer warm ischemia times (38 vs 32 and 30 min; $p = 0.002$), but there was no difference in complications between groups.

In our study, patients undergoing RPN for renal masses >4 cm had similar demographic and preoperative characteristics to patients undergoing RPN for smaller renal masses. Both groups had similar intraoperative outcomes. There was a trend toward greater blood loss for larger tumors, although this did not reach statistical significance. Similar to Simmons et al. [6], warm ischemia times in our study were longer for larger tumors (25 vs 20 min; $p = 0.011$), and we did not find a significant difference in complications based on tumor size.

Postoperative variables in this study were similar between groups. There was a trend toward a higher postoperative complication rate for tumors >4 cm (26.6% vs 8.9%), although this difference did not achieve statistical significance, likely because of the smaller number of patients in the large tumor group. Our postoperative complication rate of 26.6% for tumors >4 cm is similar to laparoscopic reports of 24% and 37% [5,6]. Two delayed urine leaks occurred in group 1 in which extensive collecting system repair was performed without preplacement of a ureteral catheter and prior to the adoption of the sliding Hem-o-lok clip technique. Patients with larger tumors had a relatively greater decline in mean estimated GFR in the short term. Possible explanations include a larger amount of tissue resected, longer warm ischemia times, and more parenchymal suturing required to complete the renorrhaphy and achieve hemostasis.

Limitations of our study include the retrospective nature of our analysis, small sample size, and single-surgeon experience. However, inclusion of different surgeons with varying experience levels may actually confound a comparison of outcomes based on tumor size because of the technical challenges of LPN for tumors >4 cm. Surgeon experience may influence choice of treatment of RCC, even as much as tumor size, demographic characteristics, or

medical health [21]. The power of our study to detect a difference between groups is limited by the smaller number of patients with tumors >4 cm. Only early oncologic and functional outcomes are available at this time, and further studies with longer follow-up are needed. Our warm ischemia times were shorter than in comparable laparoscopic series of patients with tumors >4 cm, but a potential criticism is that our total operative times were longer. The most important component of the operative time is the warm ischemia time, as this factor affects subsequent renal function. We feel that the investment of additional time for preparation to save even a few minutes of warm ischemia is time well spent. Also, we are a training program with residents and fellows who regularly perform off-clamp preparatory steps under close guidance. In addition, we treat many patients with obesity (51%), morbid obesity (11%), and prior abdominal surgery (24%), all of which likely increased our overall operative times.

Another potential criticism is that there are experienced laparoscopic surgeons who do not need to rely on robotic technology to safely and efficiently perform LPN for cT1b tumors. We acknowledge that there are highly skilled surgeons capable of performing LPN with great efficiency, even for clinical T1b tumors [5,6]. However, a recent report showed that even among surgeons with fellowship training in LPN, RPN is associated with significant improvements in operative parameters, including warm ischemia time [28]. Although most masses treated in that particular study were clinical stage T1a tumors, we feel that the purported benefits of robotic assistance can also extend to the technical challenges of LPN for clinical stage T1b renal tumors.

5. Conclusions

In our initial experience, RPN for renal tumors >4 cm is safe and feasible, showing comparable outcomes to RPN for smaller tumors, although with longer warm ischemia times. We do not necessarily advocate robotic assistance for all patients with renal masses, but it may allow select patients with larger tumors to achieve the convalescence benefits of a minimally invasive approach. Future studies with extended follow-up are necessary to determine the viability of RPN for large tumors as an effective form of treatment.

Author contributions: Craig G. Rogers had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis

Study concept and design: Patel, Siddiqui, Bhandari.

Acquisition of data: Laungani, Shrivastava, Siddiqui.

Analysis and interpretation of data: Patel, Krane.

Drafting of the manuscript: Patel.

Critical revision of the manuscript for important intellectual content: Rogers, Menon.

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