

Original article

Robot-assisted laparoscopic partial nephrectomy for tumors greater than 4 cm and high nephrometry score: Feasibility, renal functional, and oncological outcomes with minimum 1 year follow-up

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Received 29 September 2010; received in revised form 29 October 2010; accepted 29 October 2010

Abstract

Objectives: Minimally invasive robotic assistance is being increasingly utilized to treat larger complex renal masses. We report on the technical feasibility and renal functional and oncologic outcomes with minimum 1 year follow-up of robot-assisted laparoscopic partial nephrectomy (RALPN) for tumors greater than 4 cm.

Materials and methods: The urologic oncology database was queried to identify patients treated with RALPN for tumors greater than 4 cm and a minimum follow-up of 12 months. We identified 19 RALPN on 17 patients treated between June 2007 and July 2009. Two patients underwent staged bilateral RALPN. Demographic, operative, and pathologic data were collected. Renal function was assessed by serum creatinine levels, estimated glomerular filtration rate, and nuclear renal scans assessed at baseline, 3, and 12 months postoperatively. All tumors were assigned R.E.N.A.L. nephrometry scores (<http://www.nephrometry.com>).

Results: The median nephrometry score for the largest tumor from each kidney was 9 (range 6–11) while the median size was 5 cm (range 4.1–15). Three of 19 cases (16%) required intraoperative conversion to open partial nephrectomy. No renal units were lost. There were no statistically significant differences between preoperative and postoperative creatinine and eGFR. A statistically significant decline of ipsilateral renal scan function (49% vs. 46.5%, $P = 0.006$) was observed at 3 months and at 12 mo postoperatively (49% vs. 45.5%, $P = 0.014$). None of the patients had evidence of recurrence or metastatic disease at a median follow-up of 22 months (range 12–36).

Conclusions: RALPN is feasible for renal tumors greater than 4 cm with moderate or high nephrometry scores. Although there was a modest decline in renal function of the operated unit, RALPN may afford the ability resect challenging tumors requiring complex renal reconstruction. The renal functional and oncologic outcomes are promising at a median follow-up of 22 months, but longer follow-up is required. Published by Elsevier Inc.

Keywords: Partial nephrectomy; Robotic surgery; Clinical stage T1B; Renal function; Kidney cancer; Nephrometry score

1. Introduction

Open partial nephrectomy (OPN) has become the gold standard for the treatment of clinical stage T1 renal tumors [1]. The reason for this acceptance stems from 2 observations. First, the oncologic outcomes for treatment of T1a and T1b lesions compare equally when treated with radical or partial nephrectomy [2–9]. Second, recent data have demonstrated the advantage of NSS for the avoidance of

renal insufficiency as well as providing a survival advantage over radical nephrectomy for T1 renal tumors [10].

While laparoscopic partial nephrectomy (LPN) was initially utilized for small, exophytic and easily accessible renal tumors, the growing experience in laparoscopy and the adoption of robotic assistance has allowed for the treatment of larger, hilar lesions as well as multifocal tumors in the same setting [11–13]. Regardless of the surgical technique, the goals of renal surgery for T1 lesions remain the same: oncologic efficacy, renal preservation, and early convalescence.

Established advantages of robotic surgery over traditional laparoscopy include wristed articulation and the fa-

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cilitation of intracorporeal suturing while maintaining the benefits of minimally invasive surgery, such as pneumoperitoneum, decreased postoperative pain, and early convalescence [14]. While the robotic approach is seen as an “enhancement” of traditional laparoscopy in renal surgery and may shorten the learning curve for those who do not have much laparoscopic experience, robotic renal surgery may incur a higher operating cost compared with traditional laparoscopy. Nevertheless, as we gain experience managing more challenging renal tumors utilizing robotic assistance, we wished to evaluate our initial experience with robot assisted partial nephrectomy for renal cortical tumors larger than 4 cm. In this study, we report on the feasibility and renal functional as well as early oncologic outcomes of this approach.

2. Materials and methods

We have queried the Urologic Oncology database to identify patients treated with robot-assisted laparoscopic partial nephrectomy (RALPN) for tumors greater than 4 cm and a minimum follow-up of 12 months. We identified a total of 19 RALPN performed on 17 patients. Two patients underwent staged bilateral RALPN. All patients were evaluated on a protocol approved by the institutional review board.

2.1. Data acquisition and patient evaluation

Data were obtained from review of operative and pathology reports, hospital admission, discharge, and anesthesia records. The operative time was obtained from the anesthesia records from the time in the operating room to the time out of the operating room. At the time of surgery, no patients had preoperative or intraoperative suspicion of locally advanced or metastatic disease. Operative data were reported on patients in whom RALPN was successfully completed. Tumor size was assessed radiographically. The tumors were assigned a nephrometry score based on the R.E.N.A.L. tumor classification system [15]. Tumors with a score of 4–6 were considered low complexity, 7–9 moderate complexity, and 10–12 high complexity. This system allows for a more accurate and reproducible standardization of tumor size, location, and depth.

Preoperative evaluation for all patients undergoing RALPN included abdominal and chest imaging, routine laboratory analysis, and a nuclear renal scan. All studies were repeated at 3 and 12 months postoperatively and later at the discretion of the treating team. Functional outcomes were assessed using nuclear renogram, serum creatinine, and eGFR calculated by the MDRD equation [16].

2.2. Surgical technique

Cystoscopy and ureteral catheter placement were performed in all patients in the anticipation of collecting system entry to allow for intraoperative injection of methylene

blue for help in identification of the collecting system injury requiring repair. The ureteral catheter was removed at the end of each case. A standard 3-arm Da Vinci Surgical System with a transperitoneal approach was performed in 15 of 16 renal units (94%) that underwent successful RALPN and a retroperitoneal approach was performed in one. Patient positioning and port placement for RALPN were performed as previously described by our institution [11]. Laparoscopic ultrasound was used in each case to delineate the number of tumors, as well as location and depth and proximity to collecting system and vessels. Five of 16 renal units (31%) had more than 1 tumor; in these cases, surgical extirpation was begun with the smaller, exophytic tumors without hilar clamping and progressed to the larger, endophytic tumors requiring hilar clamping in most cases, as described previously in our experience of RALPN for multifocal renal masses [11].

Ten of 16 renal units (63%) in patients with hereditary or multifocal lesions were resected by enucleation, a technique previously described for the management of hereditary renal tumors at the National Cancer Institute [17]. This enucleation technique is now utilized open, laparoscopically, or robotically. Briefly, the tumor pseudocapsule was identified and a plane was developed between the tumor and the renal parenchyma. The tumor was inspected intracorporeally to ensure an intact pseudocapsule. Hilar occlusion was performed with laparoscopic bulldogs or laparoscopic Satinsky clamp only when bleeding from resection became excessive or obscured visualization. The remaining 6 of 16 renal units (37%) underwent resection with a margin of normal parenchyma. In these cases, after hilar occlusion, the tumor was resected using cold resection with robotic scissors. The tumor pseudocapsule was not visualized and a margin of normal renal parenchyma was left circumferentially surrounding the tumor.

After tumor resection, the ureteral catheter was injected with dilute methylene blue to allow precise visualization of any collecting system injury. If present, it was closed separately with running 3–0 polyglactin suture, and the renal base was oversewn with a 3–0 polyglactin suture for hemostasis. Renorrhaphy was performed using interrupted capsular 2–0 polyglactin sutures over hemostatic sealant and Surgicell (Johnson and Johnson, Piscataway, NJ) bolsters. Following renorrhaphy, the bulldog or Satinsky clamps were removed and the defect inspected for hemostasis. A 15 Fr round Jackson-Pratt drain was placed to closed bulb suction at the completion of all cases.

3. Results

Table 1 lists clinical characteristics of patients in our cohort. There was an equal gender distribution and the median BMI was 29.8 (range 19.8–40.4). Eleven of 19 RALPN (58%) were performed on patients with known hereditary syndromes, predisposing them to the risk of bi-

Table 1
Patient and tumor characteristics

Operation no./patient no.	19/17		
Staged bilateral procedures	2 (10.5%)		
Median age, y (range)	47 (26 to 76)		
Median BMI (range)	29.8 (19.8 to 40.4)		
Male (%)	9 (53)		
Surgery on the right, no. (%)	11 (58)		
Hereditary disease, no. (%)	11 (58)		
VHL	9 (47)		
BHD	1 (5)		
TS	1 (5)		
Median follow-up, mo (range)	22 (12 to 36)		
Median tumors per patient, no. (range)	1 (1 to 4)		
Median largest tumor (range)	5.0 (4.1 to 15)		
Nephrometry scores	1	2	3
R (size criteria)	0	15 (79%)	4 (21%)
E (endophytic/exophytic)	2 (10.5%)	15 (79%)	2 (10.5%)
N (nearness to sinus or calyx)	2 (10.5%)	9 (42%)	8 (47.5%)
A (anterior or posterior)	A = 12 (63%)		P = 7 (37%)
L (location relative to polar line)	5 (26%)	4 (21%)	10 (53%)
Hilar designation	6 (31.5%)		
Total nephrometry score			
4	0		
5	0		
6	1 (5.3%)		
7	2 (10.5%)		
8	2 (10.5%)		
9	8 (42.1%)		
10	4 (21%)		
11	2 (10.6%)		
12	0		
Median nephrometry score of largest tumor	9		
Largest tumor histology, no. (%)			
Clear cell	11 (58)		
Papillary type 1	4 (21)		
Chromophobe	2 (11)		
Oncocytoma	1 (5)		
Angiomyolipoma	1 (5)		

lateral, multifocal renal tumors. The remaining RALPN were performed on patients who had either a solitary solid or multiple solid tumors with unknown genetic causes. The median largest tumor size was 5.0 cm (range 4.1–15). The median R.E.N.A.L. nephrometry score of the largest tumor was 9 (range 6–11) with 12 (63%) located anteriorly and 7 (37%) posteriorly; 6 (31.5%) of these tumors had a hilar designation and 17 (89.5%) were greater than 50% endophytic. The histology of the largest tumors is also shown in Table 1.

Three RALPN (16%) required conversion to OPN. Two of these cases were converted due to excessive bleeding early in cases planned for resection of multiple masses, and the third was due to intraoperative ultrasound identification of an additional endophytic posterior lesion not appreciated on preoperative imaging that would have potentially subjected the patient to prolonged renal warm ischemia. In the

cases converted to open technique, the tumors were successfully resected without the loss of a renal unit. Of cases completed with robotic assistance five of 16 renal units (31%) had more than 1 solid tumor removed. A total of 25 solid renal masses were resected in 16 surgeries completed with robotic assistance.

Table 2 indicates preoperative outcomes for the 16 successfully completed partial nephrectomies using robotic assistance. Median operative time was 390 minutes (range 220–535). Fifteen of 16 RALPN (94%) required hilar clamping with a median ischemia time of 35.6 minutes (range 17–61). Collecting system entry with subsequent closure was performed in 8 (50%) RALPN. No patient required intraoperative blood transfusion. One patient developed a urine leak and ureteropelvic junction obstruction requiring postoperative stenting. We suspect that the case of UPJ obstruction is likely a result of repeat ureteral and hilar dissection of the previously operated kidney. Of the patients who underwent resection with margins, no positive surgical margins were identified on final pathology. None of the patients had evidence of local recurrence or metastatic disease at median follow-up of 22 months (range 12–36).

Table 3 indicates renal function outcomes. At 3 and 12 months postoperatively, there was no statistical decrease in serum creatinine or eGFR. There was, however, a statistically significant decline in median ipsilateral renal scan function of 2.5% and 3.5% at 3 months and 12 months, respectively.

4. Discussion

As the application of partial nephrectomy continues to expand, the vast majority of patients presenting with an incidental renal mass may eventually be offered some form of nephron-sparing surgery. In an effort to preserve renal preservation while maintaining the established advantages of minimally invasive surgery, urologic surgeons have expanded the role of minimally invasive surgery, applying it toward more complex renal tumors. Robotic surgery and specifically RALPN may be partly responsible for facilitating this transition. RALPN has now been shown to be

Table 2
Perioperative data (n = 16)*

Median operative time, min (range)	390 (220–535)
Median warm ischemia time, min (range)	36 (17–61)
Median estimated blood loss, mL (range)	500 (100–1600)
Hilar clamping, no. (%)	15 (94)
Collecting system entry/closure, no. (%)	8 (50)
Intraoperative transfusion, no. (%)	0 (0)
Complications (%)	1 (6)

* Data reported on successful RALPN.

Table 3
Renal function outcomes ($n = 16$)*

Median Renal Function Outcomes	Preop	Postop 3 mo	<i>P</i> value	Postop 12 mo	<i>P</i> value
Serum Creatinine, mg/dL	0.82	0.87	0.109	0.88	0.200
eGFR, mL/min	107.8	102.2	0.452	101.7	0.605
Ipsilateral renal scan function, %	49.0	46.5	0.006	45.5	0.014

* Data reported on successful RALPN.

effective for the treatment of large, multiple, and hilar renal masses [11–13]. Recent AUA guidelines have recommended strong consideration of partial nephrectomy for all T1 renal masses, regardless of overall renal function or the status of the contralateral kidney [1]. The aim of our study was to evaluate the feasibility, renal function, and early oncologic outcomes of robot assisted partial nephrectomy for renal masses greater than 4 cm. Furthermore, by assigning R.E.N.A.L nephrometry scores, we attempted to provide another measure of standardization that can be used, in addition to size, for future comparison.

We chose to report our data using the nephrometry score because currently urologists lack an accepted standard method for reporting anatomical elements of renal tumors. In 2009, Kutikov and Uzzo described R.E.N.A.L nephrometry as a novel system to quantify renal tumor size, location, and depth with the aim of providing a reproducible classification system of renal masses [15]. By having the ability to place a renal tumor in its anatomical context, the urologic surgeon may be better able to decide which surgical intervention and operative approach is most appropriate for the particular patient. In addition, the system may offer a more sophisticated and consistent way to compare results between institutions, a recurring drawback of a large number of published series.

The median R.E.N.A.L nephrometry score for the largest lesion in the present series was 9 (range 6–11), underlying the complexity of the masses removed. Examples of tumors resected using robotic assistance are displayed in Fig. 1.

Once again, as demonstrated by these images, historic reporting of only tumor size may underestimate the complexity of partial nephrectomy for a given tumor. All lesions shown in Fig. 1 are classified as T1b, but their RENAL scores are quite different. By applying measurements of location, depth, and proximity to vital surrounding structures, the nephrometry score may generate a better estimation of the surgical pitfalls that may lie ahead, regardless of technique.

Feasibility of performing robot assisted partial nephrectomy for the T1b or greater renal mass has been described recently [12]. In the LPN literature, Simmons et al. reported on 425 consecutive LPN by a single surgeon, 58 of which were for tumors greater than 4 cm [18]. In this subset, they reported an average tumor size of 6 cm, warm ischemia times of 38 minutes, and an EBL of 284 cc. Notably, as tumors became larger and more endophytic, warm ischemia times and blood loss also increased. Our cohort had similar results to both the robotic and laparoscopic series described in terms of ischemia time, complication rates, and preservation of renal function. A greater percentage of tumors removed in our study (14 of 16, 88%) were malignant by comparison. Although R.E.N.A.L nephrometry scores were not applied to these past experiences, our higher blood loss and overall operative times may be explained by the overall complexity of the RALPNs performed in this cohort. Additionally, our series represents our early experience with resecting >T1b lesions and our operative times have continued to shorten. While operative time would likely be

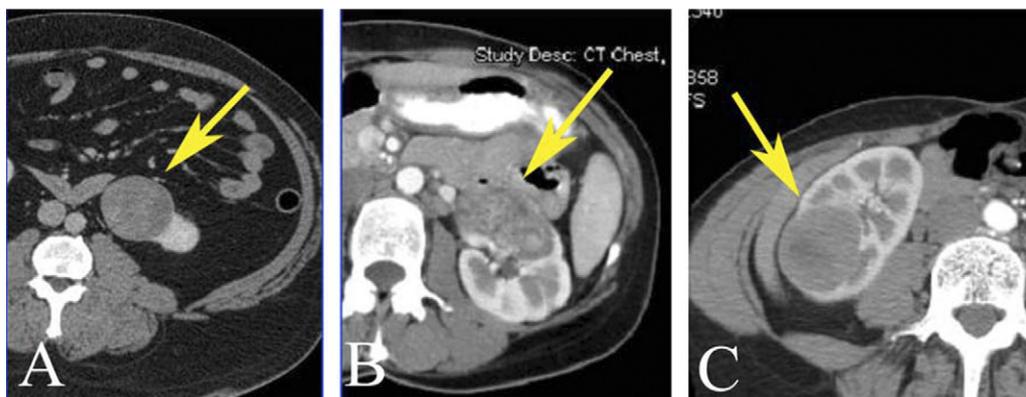


Fig. 1. Computerized tomography demonstrating variability of anatomic location and surgical complexity of various T1b renal mass and their R.E.N.A.L nephrometry score. (A) Renal mass (arrow) with nephrometry score 6a; (B) renal mass (arrow) with nephrometry score 11a,h; (C) renal mass (arrow) nephrometry score 9p. (Color version of figure is available online.)

shorter if performed open, we have demonstrated that RALPN for these tumors is safe as there was only 1 Clavien grade 3 complication in this series.

Initial concerns with minimally invasive techniques for complex partial nephrectomy rest on the foundation that prolonged warm ischemia may adversely affect renal function. Historic duration of safe, warm ischemia was thought to be 30 minutes; however, recent reports have suggested that extended warm ischemia, up to 55 minutes in 1 study, does not influence long-term renal function [19–21]. Of note, one of our patients had a warm ischemia of 61 minutes. After resection of a 6 cm lesion, a second tumor was identified adjacent to the resection site and the tumor was extirpated with robotic assistance. This was one of the earlier cases in the present series, and we feel that better judgment could have been exercised in selecting this case early in our experience with RALPN. Fortunately, the patient was 30 years old and did not experience a decline in her eGFR or a split function on postoperative renal nuclear scan. Nevertheless, we do believe that every attempt should be made for maximal renal preservation and minimizing warm ischemia time. With recent evidence suggesting that safe warm ischemia time should be no longer than 20 minutes, we have modified our technique in our most recent cases by attempting to resect tumors either without hilar clamping or utilizing “early unclamping” as described by Nguyen et al. (22).

When investigating the preservation of renal function after RALPN, it is important to consider the factors that may have influenced our findings. Although there was a significant decrease from baseline, the 2.5% and 3.5% change on ipsilateral renal scan at 3 and 12 months postoperatively in our series was lower than several published studies on partial nephrectomy [23–25]. This finding may be explained by the younger age of our cohort as well as the technique employed for surgical extirpation. Wedge resection of a renal mass may be expected to affect a larger percentage of ipsilateral renal function compared with enucleative resection, since functioning nephrons are incorporated into the resection margins. In our series, 10 of the 16 (63%) successfully completed RALPN utilized enucleation techniques while 6 (37%) were performed with a surgical margin pathologically confirmed to be completely negative. There was no statistically significant difference between the enucleation and wedge resection with regards to WIT (33.9 minutes vs. 37.8 minutes, $P = 0.28$) or the change in ipsilateral renal scan (–2% vs. –6%, $P = 0.34$), respectively. These similarities may attest to an equivalence of technique or alternatively may be explained by the complexity of the mass. Additionally, the nephrometry score was not different between the tumors resected with enucleation versus resection with margins (9.5 vs. 9, $P = 0.48$), respectively. This observation may support the use of the nephrometry score as determinant of anticipated complexity of the case and a potential surrogate predictor of the ischemia time.

The risk of operative complications and conversion to open surgery are important considerations for any mini-

mally invasive procedure, particularly when exploring new surgical techniques. In Gill’s study of 58 T1B laparoscopic partial nephrectomies, the complication and a conversion rate were 7% of 2%, respectively [18]. Historically, complication rates for other complex RALPN series have ranged from 0% to 26.6% with conversion rates ranging from 0% to 11% [11–13]. In our series, there was only 1 (6.2%) Clavien grade 3 complication (ureteral stent placement) compared with 3 (20%) Clavien grade 3 or greater complications reported by Patel et al. in the only other published series of RALPN for tumors greater than 4 cm [12]. Notably, in the series of Patel et al., only 15.4 % of tumors were greater than 50% endophytic, compared with 89.5% in the present series. Our 16% conversion rate, which may be higher by comparison, may be attributable to our high median nephrometry score (9.0), large median tumor size (5.0 cm), and multifocality (42%). With our increased experience and improved patient selection, we hope to see the number of conversions decrease.

Of importance, no RALPN in this series (including conversions) resulted in the loss of a renal unit. This further underscores that the goal of renal preservation was not compromised in our early experience. The acceptance of open conversion as a change of technique rather than a complication or technical failure is of paramount importance when attempting to perform increasingly complex minimally invasive surgeries. The preservation of the renal unit and application of sound oncologic principles should remain the primary goals of nephron-sparing surgery. In the present cohort, all patients retained their kidneys and no one had evidence of local recurrence or metastatic disease at median follow-up of 22 months.

This study has inherent limitations. It is a retrospective review and the sample size is small. This series represents a group of highly selected patients who were offered RALPN; factors such as tumor size, location, renal function, and history of prior surgeries were considered prior to offering RALPN. While the nephrometry score was reported for all lesions, the R.E.N.A.L nephrometry scoring system has not yet been validated with regards to perioperative, functional, or oncologic outcomes but is rather used to communicate the degree of difficulty of tumor resection in this cohort and for future comparisons. Regardless of these limitations, this study is the largest series to date that evaluates the feasibility as well as outcomes of RALPN for tumors greater than 4 cm with high nephrometry score and with the longest follow-up reported in the literature. Our results will hopefully add to the growing body of literature on the role of robotic assisted nephron-sparing surgery for challenging renal masses and provide useful information to physicians to help with preoperative counseling.

5. Conclusion

Performing RALPN for renal tumors greater than 4 cm with moderate or high nephrometry scores appears safe and feasible. Carefully selected patients may undergo safe resection of tumors with excellent preservation of renal function and encouraging oncologic outcomes at a median follow-up of 22 months. Longer follow-up is needed to assess long-term outcomes.

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