Published in final edited form as:

Urology. 2012 August ; 80(2): 316–322. doi:10.1016/j.urology.2012.03.043.

A Comparative Analysis of Minimally-Invasive Partial Nephrectomy Techniques in the Treatment of Localized Renal Tumors

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Abstract

Objective—To report our initial experience with robot-assisted laparoscopic partial nephrectomy compared to traditional laparoscopic partial nephrectomy.

Methods—A retrospective review of the Johns Hopkins Minimally Invasive Urological Surgery Database identified 207 consecutive patients undergoing laparoscopic or robotic-assisted laparoscopic partial nephrectomy between 2007 and 2011 by a single surgeon. Patient demographics, pathologic, operative, and peri-operative outcomes were compared between surgical techniques. Early oncologic outcomes are reported for the entire cohort.

Results—102 and 105 patients underwent LPN and RALPN, respectively. Demographic data was comparable between groups. Clinical and pathologic tumor characteristics were similar between groups, and a significant proportion (48%) of patients in each group had moderate to high complexity tumors. Patients undergoing RALPN had decreased warm ischemia time, estimated blood loss, and operative times on univariate and multivariate analysis. There was no difference in total peri-operative or significant Urologic complications between groups. Review of early oncologic outcomes revealed no local recurrences and 1 case of metastatic RCC.

Conclusions—Minimally invasive partial nephrectomy is associated with favorable peri-operative outcomes and low morbidity. RALPN appears to be associated with favorable warm ischemia times when compared to LPN.

Keywords

Renal Neoplasms; nephrectomy; robotics

INTRODUCTION

Nephron-sparing surgery has become the standard of care for management of most T1 renal masses¹. Since its introduction in 1993, laparoscopic partial nephrectomy (LPN) has emerged as an accepted alternative to the traditional open approach, given its comparable

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morbidity and oncologic outcomes and improved convalescence^{2,3}. However, widespread acceptance of LPN has been limited by the advanced technical skill set required for intracorporeal suturing and a steep learning curve⁴. Robotic assistance has been applied to LPN to mitigate these challenges and facilitate the adoption of minimally invasive nephron-sparing surgery.

Initial reports of robotic-assisted laparoscopic partial nephrectomy (RALPN) have been promising. RALPN has been shown to have a shortened learning curve as well as favorable outcomes in terms of warm ischemia time (WIT), total operative time, and estimated blood loss (EBL)^{5,6}. These benefits along with preliminary reports suggesting equivalent morbidity and oncologic outcomes to LPN have driven increased utilization of RALPN in the surgical management of small renal masses^{5–10}.

Several recent studies have directly compared peri-operative outcomes of RALPN and LPN; however, these studies have been limited by small patient numbers^{6,8,11–13}. We present a large comparative series of RALPN and LPN by a single surgeon.

MATERIALS AND METHODS

The IRB approved Johns Hopkins Minimally Invasive Urological Surgery Database was retrospectively queried for patients undergoing either LPN or RALPN by a single surgeon. Consecutive cases were evaluated. Procedures performed from 2007 – 2009 were generally performed laparoscopically without robot assistance, and those performed after 2009 were generally performed with robot assistance. Clinicopathologic data and peri-operative outcomes were compared between patients undergoing LPN and RALPN.

Patient and Tumor Characteristics

Clinical data collected included tumor size and complexity. Nephrometry scores were calculated from pre-operative computed tomography or magnetic resonance imaging and were described as low, medium, or high complexity based on numerical components 6, 7 – 9, and 10, respectively¹⁴. Pathologic data including tumor size, pathologic stage, and tumor grade were compared between groups. Stage was assigned in accordance with the AJCC 2009 TMN staging system. Tumor grade was assigned to all primary RCC with the exception of chromophobe RCC.

Peri-operative Outcomes

Data on immediate peri-operative outcomes including positive surgical margin rates, WIT, EBL, and operative time were collected and compared between surgical techniques. Operative time was determined from the anesthesia record and was defined as the time from skin incision to the completion of the surgery. Length of hospital stay (LOS) was determined from the medical record and compared between groups. Patients were routinely contacted post-operatively, and complications occurring within 30 days of surgery were identified and graded based on the Clavien system¹⁵. The rates of overall and high grade (Clavien III–IV) complications were compared between surgical modalities. Rates of significant urologic complications defined as symptomatic urine leak requiring stent placement or hemorrhage requiring transfusion or intervention were calculated between groups. Finally, to account for surgeon learning curve outcomes were compared between the most recent 50 LPNs and most recent 50 RALPNs.

Short term oncologic outcomes including overall survival, disease specific survival, and recurrence free survival are reported. Comparisons between groups were made with the Student t-test, ANOVA, and chi-squared analysis where appropriate. Multivariate regression analyses were performed to test for independent associations between the use of robotic

technology and peri-operative outcomes. Statistical calculations were performed with Stata version 11.0 (Stata Corp LP, College Station, Texas).

RESULTS

Patient and Tumor Characteristics

A total of 207 patients underwent minimally invasive partial nephrectomy by a single surgeon from 2007 – 2011. Of these, 102 (49.3%) and 105 (50.7%) patients underwent LPN and RALPN, respectively. There was no significant difference in patient demographics, comorbidities, or ASA classification between groups (Table 1). The median tumor size was 2.2 cm and 2.1 cm for patients undergoing LPN and RALPN, respectively ($p = 0.67$). Nephrometry scores were similar for patients undergoing LPN and RALPN, and 48% of patients in each group had intermediate or high complexity tumors (Table 1).

Pathologic Outcomes

Pathologic stage was similar between groups. The majority (>79%) of lesions in both groups were pathologic stage T1a ($p = 0.69$). 73.5% of patients undergoing LPN and 72.4% of patients undergoing RALPN had RCC on final pathology ($p = 0.85$). No differences in tumor grade or tumor subtypes were observed between groups (Table 2). Surgical margin rates were not statistically different for patients undergoing LPN and RALPN (1 vs. 3.8%, $p=0.19$).

Peri-operative Outcomes

Median operative time was 180 and 165 minutes for patients undergoing LPN and RALPN, respectively ($p = 0.005$). The renal artery was not occluded in 19 patients undergoing LPN and 7 patients undergoing RALPN ($p=0.01$). When considering patients undergoing partial nephrectomy with arterial clamping, the RALPN group had shorter WIT (20 vs. 15 min, $p<0.001$) and fewer patients undergoing prolonged warm ischemia time defined as WIT 30 minutes (13.6% vs. 1.0%, $p=0.001$). This difference remained significant when a patient from the LPN group with a WIT of 65 minutes (outlier) was excluded from the analysis. Median EBL was significantly less in the RALPN group (200 vs. 100 ml, $p < 0.001$), but this did not result in an increased rate of blood transfusion. Median length of post-operative hospital stay was 2 days for each group (Table 2). When considering only the most recent 50 cases for each surgical technique, patients undergoing RALPN had less EBL (150 vs. 100ml, $p=0.004$), shorter WIT (18 vs. 15.5 minutes, $p=0.01$), a similar number of patients experiencing prolonged WIT (5.1% vs. 0%, $p=0.12$), and equivalent operative times (180 vs. 177.5 minutes, $p=0.81$). On multivariate analysis, RALPN and medium tumor complexity (by nephrometry score) were statistically significant independent predictors of decreased WIT, EBL, and operative time. High tumor complexity was a statistically significant predictor of WIT but not EBL or operative time (Table 3).

No intra-operative complications occurred during either procedure. A total of 16 (15.7%) and 18 (17.2%) complications in the LPN and RALPN groups, respectively ($p=0.78$). There was no difference in the rate of significant urologic complications between groups. Patients undergoing RALPN had significantly fewer high grade (Clavien III/IV) complications (11.8% vs. 4.8%, $p = 0.006$) (Table 4). The most common complication was urine leak occurring in 6 (5.9%) and 4 (4.2%) of LPN and RALPN patients, respectively ($p=0.58$). Two LPN were converted to open partial nephrectomies and one RALPN was converted to standard LPN due to intra-operative bleeding. Another RALPN was converted to radical nephrectomy due to tumor thrombus in a segmental vein. When considering the most recent 50 cases for each surgical technique, there was no difference in total complications ($p=0.59$) or urologic complications ($p=0.24$).

Oncologic Outcomes

Follow up data was available for 94% of the 151 patients who were found to have a malignancy on final pathology. Mean follow up was 28.1 and 1.7 months for patients undergoing LPN and RALPN, respectively ($p<0.001$). No patient developed a local recurrence. One patient developed metastatic RCC 22 months after LPN. Final pathologic analysis demonstrated a 4.4 cm, high grade papillary RCC with sarcomatoid differentiation. This patient had negative surgical margins. One patient died during follow up from metastatic esophageal cancer which developed 13 months after LPN.

COMMENT

RALPN has been shown to be a safe and feasible treatment option for small renal masses¹⁶. Additionally, recent comparative studies have suggested that operative parameters such as decreased WIT favor RALPN over LPN^{5-7,9,11,12}. However, these studies are limited by the small number of patients in each cohort. Here, we present a large single institutional comparison of over 200 consecutive cases of LPN and RALPN performed by a single minimally invasive surgeon.

In the present series, peri-operative outcomes favored RALPN over LPN. In fact, on multivariate analysis RALPN was an independent predictor of decreased WIT, EBL, and operative time. Previous smaller robotic series have reported equivalent or improved WIT and EBL in patients undergoing RALPN versus LPN^{6,7,9,11,13}. Importantly, the improved operative parameters experienced by the present robotic cohort did not occur at the expense of increased operative time (180 vs. 165 minutes, $p=0.004$). This is in contrast to DeLong *et al* which reported a significantly prolonged operative time in their robotic cohort (253 vs. 352 minutes)⁶. The only previous large robotic versus laparoscopic series by Benway and colleagues also reported decreased EBL, WIT, and length of hospital stay with equivalent operative time in 129 patients undergoing RALPN by three different surgeons⁵. The current series confirms previous results by reporting favorable operative parameters.

Although we demonstrate an improvement in WIT in patients undergoing RALPN, the impact of this difference on long term renal function is unknown. However, we speculate that patients experiencing prolonged WIT are at increased risk for long term renal deterioration. As such, we further analyzed this subset of patients to identify factors associated with prolonged warm ischemia. A total of 12 patients (11 LPN and 1 RALPN) experienced prolonged WIT. When compared to the rest of the cohort, these patients had similar demographics and tumor characteristics. Review of individual operative notes revealed complex reconstruction of the nephrotomy as the etiology behind the prolonged WIT. Specifically, 7 patients required a large collecting system repair and 2 patients experienced significant back bleeding prolonging the repair. The nephrotomy reconstruction of 2 patients, including the one prolonged WIT in the RALPN cohort, was complicated by morbid obesity (BMI >40). Ease of laparoscopic suturing and improved visualization are technology-specific factors that likely contributed to a decreased number of patients experiencing prolonged WIT in the RAPN cohort. However, this difference was not observed when considering only the most recent cases suggesting surgeon experience as a critical factor in minimizing the risk of prolonged WIT. Thus, although robotic technology provides a surgeon with certain technical advantages over traditional laparoscopy, WIT may be minimized during LPN by an experienced surgeon.

RALPN has recently been described for large tumors with moderate or high complexity¹⁷. However, data comparing minimally invasive surgical techniques used to treat higher complexity tumors is sparse; previous comparisons of RALPN versus LPN have generally included small, pathologic T1a masses^{6,7,9,11}. However, tumor complexity is determined by

more than absolute size. We report successful application of robotic technology to increasingly more complex lesions. Specifically, > 50% of lesions treated robotically in the present series were classified as intermediate or high complexity based on nephrometry score. Although more complex tumors were associated with increased WIT and EBL, no patient required renal replacement therapy or a blood transfusion. Benway *et al* also report the use of RALPN in “high complexity masses⁵,” however these authors do not clearly state their definition of a high complexity lesion. We present our experience with RALPN for higher complexity tumors using a standardized system for grading complexity. Although our initial experience using RALPN to treat high complexity masses is optimistic, these patients were carefully selected and caution should be utilized when performing nephron-sparing surgery on high complexity lesions.

It is a truism that evolution of surgical technique must not occur at the expense of proven oncologic surgical principles. Consistent with this, we report a low surgical margin rate for both LPN and RALPN (1% vs. 3.8%, $p=0.19$) suggesting oncological equivalence. Although not statistically significant, an absolute larger rate of positive surgical margins was noted in patients undergoing RALPN. This difference is likely a consequence of the improved magnification of the robotic system leading to inappropriately close enucleation of the tumor early in the robotic experience. These low rates compare favorably to previous reports of robotic, open, and laparoscopic partial nephrectomy^{5,18–20}. Furthermore, at a median follow up of 3 months no patient with a positive margin has experienced a local or systemic recurrence. This is consistent with the findings of Yossepowitch and colleagues demonstrating that the presence of a focally positive margin did not increase the risk of disease recurrence or metastatic progression²¹. When considering the entire cohort, no patient died of RCC and no patient experienced a local recurrence. These short term oncologic outcomes compare favorably to contemporary LPN series and require further follow-up^{2,22}.

In the present experience, patients undergoing RALPN and LPN experienced equivalent overall complication rates. However, we observed a significant increase in the rate of high grade (Clavien III/IV) complications in the LPN cohort. Urine leak requiring ureteral stenting was responsible for 3/5 and 2/12 of the high grade complications in the RALPN and LPN cohorts, respectively. Pseudoaneurysms requiring embolization accounted for 2/5 and 5/12 high grade complications in the RALPN and LPN cohorts, respectively. As there were a similar number of urine leaks and pseudoaneurysms in each group, the significant increase in high grade complications among LPN patients was driven primarily by medical processes including pulmonary embolism, cardiac arrhythmia, and 2 cases of over-narcotization. Interestingly, no difference was noted in the rate of overall complications, high grade complications, or procedure-specific complications when considering only the most recent cases. Although we cannot make a definitive statement regarding relative safety of the two procedures, our experience suggests either procedure can be performed safely with acceptable complication rates. Notably, the overall complication rates experienced by both groups are similar to contemporary reports ranging from 6.1 to 20%^{5,13,20,23}.

The advantages offered to surgeon and patients alike by robotic technology must always be weighed against the cost of the technology itself. We previously demonstrated RAPN is associated with a small to moderate increase in cost depending on the percent of ideal institutional utilization of the robot²⁴. In the present analysis, we have demonstrated that both LPN and RALPN can be performed safely, but robotic technology may offer certain objective advantages over traditionally laparoscopy. However, the impact of improved WIT and EBL on long term patient outcomes is unknown. Whether this cost premium is warranted will be determined by the impact of robotic technology on long term renal function and oncologic outcomes.

As with any consecutive surgical series, the present results may be influenced by a surgeon's learning curve. To account for this potential confounding factor, we compared the peri-operative outcomes of the most recent 50 cases for each surgical technique. This analysis confirmed that patients undergoing RALPN experienced improved WIT and EBL compared to those undergoing LPN. However, operative times and complication rates were equivalent in the most recent cases. We have previously demonstrated a learning curve of approximately 25 cases for minimally invasive partial nephrectomy¹². Therefore, these results represent cases done after the initial learning curve and are likely attributable to differences in surgical technique. Despite our additional analysis, early experience with traditional laparoscopy likely impacts the results of more recent cases performed with robotic assistance, and the potential for experience bias still exists.

There are several other limitations of our study that deserve mention. First, as a retrospective evaluation there is the potential for selection bias affecting outcomes independent of technique. However, we have attempted to minimize this risk by controlling for disease and notable patient characteristics. Use of either technique was primarily dependent on availability of technology rather than patient factors. Furthermore, as a single surgeon experience, we avoid confounding effects of the skill sets and learning curves of different surgeons. Second, longer follow-up is needed to determine the true impact of minimally invasive partial nephrectomy on ultimate renal outcome and long term oncologic control. Finally, we report the experience of a high-volume, minimally invasive surgeon which may limit the generalizability of the results. Nonetheless, using multivariate analysis, our results suggest that RALPN may offer an advantage over LPN in certain peri-operative parameters. Further study of the clinical benefits and accessibility of these techniques for the noble goal of minimally invasive nephron-sparing surgery is clearly warranted.

CONCLUSIONS

Minimally invasive partial nephrectomy is associated with favorable perioperative and early oncological outcomes. On average, patients undergoing RALPN had shorter WIT, less EBL, and equivalent surgical margin rates. No difference in operative time was observed when accounting for surgeon learning curve. Our data suggest clinical benefits to RALPN, however this requires confirmation in additional, large scale investigation.

Acknowledgments

The project described was supported by Award Number T32DK007552 from the National Institute of Diabetes and Digestive and Kidney Diseases. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institute of Diabetes and Digestive and Kidney Diseases or the National Institutes of Health.

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Table 1

Demographic data and clinical tumor characteristics of 207 patients undergoing minimally invasive partial nephrectomy by one surgeon from 2006 – 2011.

	LPN (n = 102)	RALPN (n = 105)	P-value
Variable			
Age (Median)	56 (25 – 81)	61 (27 – 80)	0.70
Male Sex (%)	61.7	54.3	0.28
Mean BMI	30.9	29.2	0.06
Race (%)			0.36
White	80.4	85.6	
Black	13.7	7.7	
Other	5.9	6.7	
Comorbidities (%)			
Hypertension	62.7	59.4	0.63
Diabetes	24.5	18.0	0.26
Smoking History	37.3	43.0	0.41
Family History of RCC (%)	2.9	4.8	0.18
Prior Abdominal Surgery (%)	54.9	46.7	0.24
ASA (%)			0.62
1 or 2	47.5	51	
3 or 4	52.5	49	
Tumor size (cm)	2.2 (0.5 – 7.7)	2.1 (0.9 – 6.9)	0.93
Laterality (%)			0.57
Right	53.9	56.2	
Left	46.1	42.9	
Bilateral	0	0.9	
Nephrometry Risk Group (%)			0.54
Low	52	46.5	
Medium	45.3	47.7	
High	2.7	5.8	

Table 2

Pathologic and Operative data of patients undergoing laparoscopic partial nephrectomy and robot-assisted laparoscopic partial nephrectomy

	LPN (n = 102)	RALPN (n = 105)	P-value
Pathologic Parameter			
Stage (%)			0.69
T1a	79.7	81.6	
T1b	13.5	10.5	
T2	0	1.3	
T3a	6.8	6.6	
RCC (%)	73.5	72.4	0.85
Clear Cell	59.5	67.1	
Papillary	29.7	14.5	
Chromophobe	9.5	14.5	
Mixed	1.4	1.3	
AML	9.8	7.6	
Oncocytoma	9.8	11.4	
Benign (other)	7.8	6.7	
Metastases	0	1.9	
Grade (%)			0.68
1 or 2	70.6	73.8	
3 or 4	29.4	26.2	
Operative Parameter			
Median Operative Time (min)	180 (100 – 420)	165 (100 – 330)	0.005
Median EBL (mL)	200 (50 – 1700)	100 (50 – 500)	<0.001
Median WIT (min)	20 (8 – 65)	15 (6 – 34)	0.02
Prolonged WIT (%)	13.6	1.0	0.02
Transfusion (%)	4.9	0	0.14
Positive Margins (%)	1	3.8	0.19
Median LOS (days)	2 (1 – 8)	2 (1 – 8)	0.49

Table 3

Multivariate regression analysis for warm ischemia time (WIT), estimated blood loss (EBL), and operative time.

Variable	WIT		EBL		Operative Time	
	β - Coeff	p-value	β - Coeff	p-value	β - Coeff	p-value
Age	-0.05	0.37	0.43	0.75		
Male Sex	-1.2	0.13	-16.48	0.57	-19.14	0.02
Race						
Caucasian	-	-	-	-	-	-
African - American	-0.24	0.90	-35.38	0.41	-8.66	0.49
Other	-0.09	0.97	32.77	0.56	-17.45	0.28
BMI	-0.01	0.95	2.28	0.30	0.98	0.13
Robotic Approach	-5.34	<0.01	-112.21	<0.01	-19.36	0.02
Nephrometry Complexity						
Low	-	-	-	-	-	-
Medium	3.25	<0.01	66.43	0.02	20.23	0.02
High	6.27	0.03	7.04	0.92	34.34	0.09

Table 4

Complications in patients undergoing minimally invasive partial nephrectomy.

	LPN N = 102	RALPN N = 105	P-value
Variable			
Complications (%)			
Any	15.7	17.1	0.78
Urologic	11.8	5.7	0.12
Clavien Grade (%)			0.006
1 or 2	3.9	12.4	
3 or 4	11.8	4.8	
Conversion (n)	2	2	0.98