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ORIGINAL ARTICLE

Robotic partial nephrectomy shortens warm ischemia time, reducing suturing time kinetics even for an experienced laparoscopic surgeon: a comparative analysis

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Abstract

Objectives Laparoscopic and robotic partial nephrectomy (LPN and RPN) are strongly related to influence of tumor complexity and learning curve. We analyzed a consecutive experience between RPN and LPN to discern if warm ischemia time (WIT) is in fact improved while accounting for these two confounding variables and if so by which particular aspect of WIT.

Methods This is a retrospective analysis of consecutive procedures performed by a single surgeon between 2002–2008 (LPN) and 2008–2012 (RPN). Specifically, individual steps, including tumor excision, suturing of intrarenal defect, and parenchyma, were recorded at the time of surgery. Multivariate and univariate analyzes were used to evaluate influence of learning curve, tumor complexity, and time kinetics of individual steps during WIT, to determine their influence in WIT. Additionally, we considered the effect of RPN on the learning curve.

Results A total of 146 LPNs and 137 RPNs were included. Considering renal function, WIT, suturing time, renorrhaphy time were found statistically significant differences in favor of RPN ($p < 0.05$). In the univariate analysis, surgical procedure, learning curve, clinical tumor size, and RENAL nephrometry score were statistically significant predictors for WIT ($p < 0.05$). RPN decreased the WIT on average by approximately 7 min compared to LPN even when adjusting for learning curve, tumor complexity, and both together ($p < 0.001$).

Conclusions We found RPN was associated with a shorter WIT when controlling for influence of the learning curve and tumor complexity. The time required for tumor excision was not shortened but the time required for suturing steps was significantly shortened.

Keywords Kidney cancer · Laparoscopy · Nephrectomy · Renal cell carcinoma · Robotics

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Introduction

Nephron sparing surgery (NSS) is the new accepted standard of care for treatment of the small renal mass [1]. Robotic-assisted partial nephrectomy (RPN) has recently been reported to improve the outcomes of laparoscopic partial nephrectomy (LPN) by possible reduction in warm ischemia time (WIT) [2, 3]. LPN is technically challenging and has a steeper learning curve because it requires not only precise tumor margin resection but also complex and time-dependent renal hemostasis and reconstruction [2]. It is possible that RPN decreases the learning curve [4] and has been associated with increased utilization of partial nephrectomy. Pierorazio et al. [5] reported that increase in nephron sparing surgery has been facilitated by robotic technology. However, results of partial nephrectomy are strongly influenced by tumor size and complexity, and both partial nephrectomy and laparoscopic surgery are strongly under the influence of the learning curve [6, 7]. Thus, any study evaluating outcomes of these approaches may be strongly biased by these factors unless they are accounted for during data collection and analysis. It is also unclear how the addition of the robotic interface may improve the laparoscopic approach to partial nephrectomy, and specific data in this regard may help future robotic applications. We thus analyzed a single surgeon's comparative experience between RPN and LPN, while accounting and adjusting for the learning curve, tumor complexity, and analyzed time kinetics of individual steps during WIT, to determine whether WIT is truly shortened when accounting for these factors and, if so, to define which specific steps are shortened by the robotic approach.

Patients and methods

This study is a retrospective analysis of all consecutive procedures (LPN or RPN) performed by a single surgeon (S.F.M.) between 2002 and 2012. NSS was offered to all patients meeting accepted elective and imperative criteria. [1] LPN was offered from 2002 until 2008, while RPN was offered from 2008 onward. Cases performed without hilar clamping and those converted to open surgery or radical nephrectomy were excluded. Other standard demographic, perioperative, and renal function data were collected. Learning curve was defined as case number and represented as a continuous variable. The learning curve was defined as the number of cases required to consistently perform RPN with WIT, as compared to the end of LPN series. Specifically, individual steps, including tumor excision (EXC), suturing of intrarenal vessels and collecting system (INTRA), and renorrhaphy (REN), were recorded at the time of surgery in 190 procedures. The Institutional Review Board approved this retrospective study.

Surgical technique

For LPN, similar principles as established by Novick and Gill's group [8] were utilized. For RPN, the same steps were performed as for LPN, modified where needed for a robotic approach. A 2-arm approach with a 0° camera was used as a standard, utilizing monopolar scissors in the right hand which was exchanged for a needle driver during suturing, and Prograsp forceps in the left hand. For hilar tumors, a 3-arm approach was used with the addition of a Maryland bipolar. A single 12-mm assistant port was placed routinely, and in the very obese, an additional 5-mm assistant port was placed for bowel retraction. Bulldog placement by the assistant was performed until recently; we have now obtained bulldogs allowing placement with a robotic Prograsp (Scanlan International, St. Paul, MN). The artery was always clamped, and for tumors with significant central extension, we also clamp the vein. Placement of oxidized cellulose bolsters, injection of a collagen matrix, and placement of a drain were done selectively and not routinely. For follow-up, patients were seen 4–6 weeks postoperatively, and those with pT1a tumors were followed annually with chest imaging and comprehensive laboratory studies, with abdominal scanning performed 1–3 years after surgery.

Data collected included standard patient demographics, indication for nephron sparing (elective vs. imperative), tumor data (side, radiographic and pathologic size, RENAL nephrometry score [9]), renal function data (serum creatinine level, estimated glomerular filtration rate [eGFR] based on the Modification of Diet in Renal Disease calculation, percentage of parenchymal volume preserved), surgical data (estimated blood loss, blood transfusions, conversions, surgery time, WIT, and individual time kinetics of EXC, INTRA, and REN), pathologic data (tumor histology, stage classification, size of normal margins, positive surgical margins), postoperative data (length of hospital stay, complications using Clavien classification [10], number of days until drain removal). The percentage of parenchyma preserved was calculated by visual estimate.

Statistical analysis

Summary statistics were used to describe the demographic and clinical characteristics for all patients and for the two surgical procedure cohorts. Wilcoxon rank-sum test and Pearson's Chi-square test (or Fisher's exact test) were used to determine whether there were differences in demographic and clinical characteristics between surgical procedures. We used a univariate linear regression to model WIT as a function of the surgical procedure (LPN vs. RPN) and other potential covariates. Full and reduced multivariate linear regressions were used to model the WIT as a function of the surgical procedure while adjusting by covariates. Linear regression was used to evaluate the effect of the learning curve (based on case number) and tumor complexity on WIT, and the effect of robotic-assisted technique on learning curve. Statistical analysis was performed using Stata/SE version 12.0 statistical software (StataCorp LP, College Station, TX).

Results

Of all 309 patients, 291 had the procedure finished as a minimally invasive partial nephrectomy. No-clamp technique was used in seven cases and these were excluded. We had 13 cases converted to open partial nephrectomy, six converted to radical nephrectomy, and one converted to open radical nephrectomy. The majority of these conversions occurred after Gerota's fascia was approached and

Table 1 Summary of clinical, tumor, pathological, perioperative, and renal functional characteristics by type of procedure

Preoperative clinical	Surgery type				*p* Value
	Laparoscopy ($n = 146$) Median (min–max)		Robotic ($n = 137$) Median (min–max)		
Age at surgery (years)	62.0 (24.0–86.0)		60.3 (29.8–84.6)		0.409[a]
BMI (kg/m^2)	29.0 (18.8–48.7)		30.4 (16.6–52.7)		0.226[a]
Clinical tumor size (cm)	2.5 (0.9–7.8)		2.7 (1.0–7.0)		0.065[a]
Pre-op serum creatinine (mg/dL)	1.0 (0.0–2.6)		0.9 (0.5–1.6)		<0.001[a]
Pre-op MDRD (mL/min/173 m^2)	73.2 (0.0–144.4)		87.3 (41.2–141.1)		<0.001[a]
Follow-up (months)	53.5 (0.0–119.0)		13.0 (0.0–49.0)		<0.001[a]
	N	(%)	*N*	(%)	
Females	54	(37.0)	71	(51.8)	0.012[b]
White	112	(76.7)	104	(75.9)	0.874[b]
Right side	76	(52.1)	73	(53.3)	0.836
ASA Classification 3	97	(66.4)	87	(63.5)	0.067[c]
Median RENAL nephrometry score (min–max)		7.0 (4.0–10.0)		7.0 (4.0–10.0)	0.657[a]
RENAL scores, individual	*N*	(%)	*N*	(%)	
Radius-1	125	(85.6)	112	(81.8)	0.216[c]
Radius-2	14	(9.6)	23	(16.8)	
Exo/endo-1	71	(48.6)	67	(48.9)	0.027[c]
Exo/endo-2	68	(46.6)	58	(42.3)	
Nearness-1	64	(43.8)	62	(45.3)	0.380[b]
Nearness-2	22	(15.1)	14	(10.2)	
Anterior	60	(41.1)	79	(57.7)	0.489[b]
Location-1	54	(37.0)	54	(39.4)	0.355[b]
Location-2	32	(21.9)	39	(28.5)	
Hilar	18	(12.3)	29	(21.2)	0.046[b]
Pathologic	*N*	(%)	*N*	(%)	
Positive surgical margins	2	(1.4)	2	(1.5)	0.999[c]
Malignant histology	113	(77.4)	118	(86.2)	0.058[b]
Clear cell histology	73	(50.0)	96	(70.1)	0.001[c]
pT1a Stage	132	(90.4)	108	(79.4)	0.009[c]
Perioperative	*N*	(%) or median (min–max)	*N*	(%) or median (min–max)	
Clamp method—artery alone	52	(35.6)	50	(36.5)	<0.001[c]
Clamp method—both artery and vein	43	(29.5)	77	(56.2)	
EBL (mL)		100.0 (25.0–650.0)		125.0 (10.02–200.0)	0.284[a]
Total OR time (min)		195.0 (115.0–285.0)		192.5 (105.0–325.0)	0.655[a]
Transfusions	1	(0.7)	3	(2.2)	0.357[c]
Clavien score (CS)					0.433[c]
I	3	(25.0)	8	(53.3)	
II	8	(66.7)	6	(40.0)	
IIIb	1	(8.3)	1	(6.7)	
Ischemia time and renal function	Median (min–max)		Median (min–max)		
Warm ischemia time	26.0 (13.0–55.0)		20.0 (10.0–41.0)		<0.001[a]
Excision (min)	6.0 (4.0–12.0)		6.6 (2.0–15.0)		0.505[a]
Suturing (min)	10.0 (4.0–29.0)		7.0 (2.0–17.0)		<0.001[a]

Table 1 continued

Ischemia time and renal function	Median (min–max)	Median (min–max)	
Renorrhaphy (min)	9.0 (2.0–21.0)	6.0 (1.0–16.0)	<0.001[a]
Post-op serum creatinine (mg/dL)	1.1 (0.0–3.1)	0.9 (0.0–1.6)	<0.001[a]
Post-op MDRD (mL/min/173 m^2)	68.9 (0.0–113.7)	78.0 (0.0–146.5)	<0.001[a]
Last follow-up serum creatinine (mg/dL)	1.0 (0.0–3.2)	0.9 (0.0–50.0)	<0.001[a]
Last follow-up MDRD (mL/min/173 m^2)	69.7 (0.0–131.3)	79.4 (0.0–158.9)	<0.001[a]
% Kidney preserved	85,0 (25–97)	79.5 (50–95)	<0.001[a]

[a] Wilcoxon rank-sum

[b] Pearson's Chi-square

[c] Fisher's exact test

upon realization that tumor number or complexity was higher than revealed on imaging. There were five cases converted during or after the partial procedure, one due to positive margins on frozen section. Thus, for the final analyses, we studied 283 procedures with hilar clamping technique.

Table 1 shows the summary statistics for all 283 procedures and for the two surgical procedure cohorts (146 LPN, 137 RPN). Prior to 2008, 146 LPNs were performed after exclusionary criteria; we converted to RPN exclusively in 2008. Tumor size, percentage of kidney parenchyma preserved, American Society of Anesthesiologists (ASA) physical status classification, and overall histology were not significantly different between the LPN and RPN groups ($p > 0.05$). Considering serum creatinine level and eGFR (1 month postoperatively, and at last follow-up), suturing time, renorrhaphy time were found to have statistically significant differences ($p < 0.05$). WIT was significantly different between the LPN and RPN (26.0 vs. 20.0, respectively; $p < 0.001$).Statistically significant improvement was seen with suturing steps during WIT (Table 1).

In the univariate analysis, surgical procedure, learning curve, clinical tumor size, and RENAL nephrometry score were statistically significant predictors for WIT ($p < 0.05$; Table 2a). After controlling for all the potential predictors from the univariate analysis ($p < 0.25$), we found that surgical procedure, learning curve, clinical tumor size, nephrometry score were statistically significant predictors for WIT ($p < 0.05$). After we eliminated variables using backward selection methods ($p < 0.05$), we found that surgical procedure, learning curve, clinical tumor size, nephrometry score, and partial nephrectomy indication were still significant predictors of WIT (Table 2a).

Additional regression models were performed for WIT and surgical procedure while adjusting for learning curve and tumor complexity (Table 2a, b and Fig. 1). There was a significant WIT difference while adjusting for learning curve (model 1, Table 2b) and while adjusting for tumor complexity (model 2, Table 2b). Including both learning curve and tumor complexity maintained the benefit of RPN (model 3, Table 2b). According to linear regression lines of LPN and RPN (Fig. 1), the WIT reached by 140 cases of LPN was achieved earlier with only 40 cases, showing the influence of robotic technology on the learning curve.

Discussion

Compared to a laparoscopic approach, the use of a robotic approach significantly reduces the WIT, even when accounting for learning curve and tumor complexity, both of which are significant confounders of similar prior analyses. Our data show that the decrease in the WIT during RPN is appreciated from a significant decrease in the suturing steps; there was no significant difference in the time for tumor excision between LPN and RPN. Previously, the advantage of the 3-dimensional view and wristed robotic motion was only conceptual. Evaluation of the timing kinetics in this series validates that the advantage may be attributed to the robotic system for the complex maneuvers needed for suturing. Overall, there was no significant difference in nephrometry score between our robotic and laparoscopic cohorts. However, there were more endophytic, central, and hilar tumors in the RPN group which would be expected to adversely affect outcomes and thus reducing the benefit of the robotic approach.

While long-term oncologic outcomes are yet to be evaluated, it has been shown that the robotic approach is comparable to the laparoscopic approach in the perioperative setting with regard to WIT and pathologic outcomes [11–16]. The majority of published studies have shown that RPN offers a decrease in WIT [3], while others have shown the WIT comparison to be equivocal [14]. A paucity of published articles has compared RPN versus LPN using a standardized system to measure complexity (e.g., nephrometry score), incorporation of learning curve, or the time kinetics of individual steps during WIT.

Table 2 Linear regression for (a) warm ischemia time (WIT), and (b) WIT and learning curve

	Univariate analysis			Full multivariate analysis*			Reduced multivariate analysis**		
	β	95 % CI for β	p Value	β	95 % CI for β	p Value	β	95 % CI for β	p Value
(a) Linear regression for WIT									
Surgery									
Laparoscopic (ref)									
Robotic	−6.70	(−8.49, −4.90)	<0.001	−8.38	(−10.02, −6.74)	<0.001	−7.83	(−9.37, −6.29)	<0.001
Learning curve	−0.06	(−0.08, −0.04)	<0.001	−0.08	(−0.10, −0.06)	<0.001	−0.08	(−0.10, −0.06)	<0.001
Age at the time of surgery	−0.01	(−0.07, 0.09)	0.801						
BMI	0.12	(0.04, 0.29)	0.128	0.11	(−0.02, 0.24)	0.110			
Clinical tumor size (cm)	1.73	(0.99, 2.46)	<0.001	1.84	(1.15, 2.52)	<0.001	2.38	(1.77, 2.97)	<0.001
Path tumor size (cm)	−0.01	(−0.02, 0.01)	0.361						
RENAL nephrometry score	0.94	(0.36, 1.52)	0.002	0.54	(0.03, 1.05)	0.040			
% Kidney preserved	−0.03	(−0.12, 0.07)	0.261	−0.07	(−0.14, 0.01)	0.104			
Side of surgery									
Right (ref)									
Left	0.34	(−1.63, 2.30)	0.737						
Hilar									
No (ref)									
Yes	−0.40	(−306, 2.26)	0.768						
(b) Linear regression for WIT and learning curve									
Model 1									
Surgical technique									
Laparoscopic (ref)									
Robotic	−6.83	(−8.45, −5.21)	<0.001						
Learning curve	−0.07	(−0.08, −0.05)	<0.001						
Model 2									
Surgical technique									
Laparoscopic (ref)									
Robotic	−6.16	(−7.87, −4.45)	<0.001						
RENAL score	0.91	(0.39, 1.42)	0.001						
Model 3									
Surgical technique									
Laparoscopic (ref)									
Robotic	−6.73	(−8.33, −5.13)	<0.001						
Learning curve	−0.06	(−0.08, −0.04)	<0.001						
RENAL Score	0.90	(0.42, 1.38)	<0.001						

The beta (β) indicates the reduction (negative value) or addition (positive value) of ischemia time based on the variable analyzed

* Excludes variables with $p > 0.25$ on the univariate analysis

** Excludes variable with $p \geq 0.05$ using backward elimination method

The majority of patient and tumor-related variables are unmodifiable, and the WIT is the most important factor the surgeon can alter in order to achieve better functional outcomes. Although the RPN and LPN are almost identical, our evaluation of time kinetics showed no significant difference in the time for tumor excision between both techniques but RPN decreased the time to perform complex maneuvers during suturing of the vessels/collecting system and renorrhaphy. These data show that even with the influence of the learning curve and tumor complexity, WIT is still favorably reduced by RPN, particularly by shortening the suturing steps during WIT. Despite increasing tumor complexity, we still appreciated a difference in WIT between RPN and LPN. Data from 2009 support this inference by showing that WIT was significantly lower for RPN in more complex tumors [11]; complexity in that study, however, was only defined as a need for calyceal repair during surgery and not by the more objective

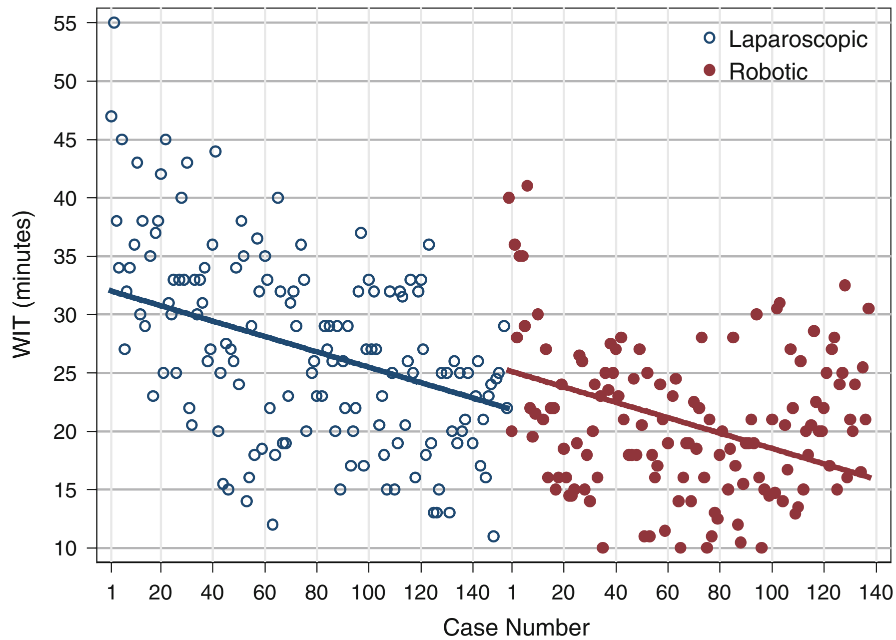

Fig. 1 Linear regression lines of laparoscopic and robotic partial nephrectomy, showing the influence of the learning curve as based on case number

measure using nephrometry. Given the potential for long-term renal function damage caused by ischemia, this reduction in time may be meaningful in the long term and may, with the minimally invasive benefit, justify the added cost of the robotic approach.

The primary limitation of our study is that it was a retrospective analysis with potential unrecognized selection bias. Confounders and bias were minimized by the consecutive nature of our cohorts; all surgeries were switched from laparoscopic to robotic. There were some gradual technical modifications that occurred over the course of LPN and RPN, which cannot be pinpointed as to the exact transition of the change, and may have influenced the results. Additionally, we adjusted in the multivariable model any potential confounders, thus accounting for all measurable differences between the two approaches. Our use of linear regression to develop the effect of the learning curve may also be criticized. We developed the linear regression of the initial robotic cases against the initial cases of LPN. As robotic surgery has improved the laparoscopic approach, comparing these regressions head to head may exaggerate the true difference in WIT.

Regarding our analysis in linear regression, the WIT plateau was reached faster in RPN, with only around 40 cases. The authors understand recognize that experience accumulated over the laparoscopic cohort biases the data. However, we do believe that current robotic systems provide differences in optically magnified three-dimensional imaging and a greater range of fully articulated wristed-instrument motion, allowing more facile and efficient ambidextrous manipulation [17, 18]. This study must be viewed in light of its limitations, because it is a cohort observational study with no randomization; all surgeries were done by one surgeon with laparoscopic experience but still requiring a learning curve for the robotic approach. However, this bias is common in nearly all studies comparing RPN with LPN, such as those from several centers of experience as Lavery et al. [19] and as reviewed by Aboumarzouk et al. [2]. These limitations could be solved by a prospective, randomized, multi-institutional trial with robotically naïve surgeons in order to measure the true difference after the learning curve. These findings may also not translate to a surgeon directly converting from open to RPN, and such data could prove meaningful for the larger picture of increasing utilization of partial nephrectomy in the urologic community. RPN has continued to prove a safe alternative to LPN. RPN also appears to offer the advantage of decreased WIT. As the techniques advance and comfort with the robotic approach increases, we may expect to see more common use of nephron sparing techniques with more complex tumors and with even further reduction in WIT.

Conclusion

This study found that RPN had satisfactory perioperative outcomes and was similar to LPN in terms of complications, pathological outcomes, and short-term outcomes. Despite learning curves for robotic urologic surgery are subjective and based on non-validated metrics, we found RPN was associated with a shorter WIT when controlling for influence of the learning curve and tumor complexity. The time required for tumor excision was not shortened but the time required for suturing steps was significantly shortened. Studies assessing WIT should account for the influence of the learning curve and objective measures of tumor complexity when analyzing the results of technical advances. Only a randomized trial with longer follow-up can provide definitive results.

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Conflict of interest The authors declare that there is no conflict of interest.

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