Original Article

Impact of learning curve on the perioperative outcomes following robot-assisted partial nephrectomy for renal tumors

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ABSTRACT

Introduction: Robot-assisted partial nephrectomy (RAPN) is an established, minimally invasive technique to treat patients with renal masses. The aim of this study was to assess the learning curve (LC) of RAPN, evaluate its impact on perioperative outcomes following RAPN and to study the role of surgeon experience in achieving "trifecta" outcomes following RAPN.

Methods: We prospectively analyzed the clinical and pathological outcomes of 108 consecutive patients who underwent RAPN for renal tumors from January 2012 to December 2016 by a laparoscopy trained surgeon with no prior robotic experience. We used warm ischemia time (WIT) <20 min, operative time <120 min, and blood loss <100 ml as endpoints for plotting the LCs. Trifecta was analyzed in relation to our LC.

Results: Surgeon experience was found to correlate with WIT, operative time, and blood loss. Overall 18.5% of patients developed complications. Complication rate reduced with increasing surgeon experience. LC was 44 cases for WIT ≤20 min, 44 cases for operative time <120 min, and 54 cases for blood loss <100 ml. Trifecta outcome was achieved in 67.6% patients overall and was found to correlate with increasing surgeon experience. Improvement in trifecta outcomes continued to occur beyond the LC.

Conclusions: RAPN is a viable option for nephron-sparing surgery in patients with renal carcinoma. For a surgeon trained in laparoscopy, acceptable perioperative outcomes following RAPN can be achieved after an LC of about 44 cases. Increasing surgeon experience was associated with improved "trifecta" achievement following RAPN.

INTRODUCTION

Partial nephrectomy is currently considered the gold standard of treatment for tumors <4 cm (T1a).[1,2] For such tumors, partial nephrectomy is shown to have similar perioperative complications and cause-specific survival when compared with radical nephrectomy (RN).[3-5]

Laparoscopic partial nephrectomy (LPN) is a technically challenging procedure requiring a long learning curve (LC) to reach acceptable warm ischaemia times (WITs) and perioperative complications.[6] Since its introduction in 2004 by Gettman *et al.*,[7] robot-assisted partial nephrectomy (RAPN) using the da Vinci Surgical System has been steadily gaining acceptance as a viable alternative to both open and LPN for patients with small renal masses amenable to nephron-sparing surgery.[8,9]

Many centers across the globe have demonstrated the feasibility of RAPN for more complex cases, including hilar, endophytic, and multiple tumors.[7,10-14] However, it has been suggested that prior robotic experience and familiarity with the robotic platform are important for successful application of RAPN.[10,12] Urological procedures

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are the most common procedures performed robotically in India.[15]

The primary aim of this study was to assess the LC of RAPN and to evaluate its impact on the perioperative outcomes of patients undergoing RAPN. The secondary aim was to evaluate the role of surgeon experience in the achievement of "trifecta" outcomes following RAPN.

METHODS

We prospectively collected clinical data for 108 patients who underwent a transperitoneal RAPN for parenchymal renal tumors using the da Vinci Surgical System in our department from January 2012 to December 2016 (4 years). The present study was approved by the Institutional Ethical Review Board. Informed consent was obtained from each patient before the respective robotic surgery was conducted.

Inclusion and exclusion criteria

All patients presenting with renal tumors were assessed for feasibility of partial nephrectomy. Patients classified as having T1a and T1b tumors based on preoperative imaging studies who subsequently underwent RAPN were included in the study.

Patients who were excluded from the study included:

1. Patient undergoing partial nephrectomy through open or pure laparoscopic approach
2. Patients with locally advanced tumors, and patients with metastatic renal tumors
3. Patients undergoing partial nephrectomy for other indications such as renal calculous disease, nonfunctioning renal moiety of a duplex renal system, renal trauma, or renovascular hypertension due to a branch renal artery stenosis.

Study protocol

A prospectively maintained database of all patients undergoing RAPN is available at our institution. For every patient, the preoperative characteristics assessed were age, gender, tumor location, laterality, and estimated glomerular filtration rate (GFR). All patients had either a contrast-enhanced computed tomography or magnetic resonance imaging done as a part of the workup for renal tumor. R. E. N. A. L. Nephrometry Score (RNS) was calculated based on the criteria proposed by Kutikov *et al*. and patients were divided into low (4–6), medium (7–9) and high (10–12) complexity tumor groups.[16] We also used the preoperative aspects and dimensions used for anatomical (PADUA) classification of renal tumors in our study based on the criteria proposed by Ficarra *et al*.[17] PADUA scores were categorized into low (6–7), medium (8–9) and high (≥10) complexity tumors.[17]

Intraoperative characteristics assessed included operative time, console time, WIT, estimated blood loss (EBL), complications, and hospital length of stay. The console time was defined as the total time during which the surgeon performed the procedure using the robotic system. The operation time was defined as the time between the initial skin incision and the completion of wound closure. Postoperative outcomes assessed included surgical margin status, pathological results, GFR, bleeding complications, and urine leak. Thirty- and 90-day complications were collected. We limited our analysis to 90 days, assuming that most perioperative complications will occur within that time frame. Complications were classified were classified using the Clavien-Dindo Classification of surgical complications.[18]

All the procedures were performed using the standard robotic technique, which is described elsewhere.[7,13]

We used the console time, operative time, blood loss, WIT, "trifecta" achievement, and complication rate to assess our LC. "Trifecta" achievement was defined as WIT of ≤25 min, negative surgical margins and absence perioperative complications as per the criteria proposed by Hung *et al*.[19] The objective parameters for defining our LC included operative time of <120 min, EBL <100 ml, and WIT <20 min. The learning curves were plotted using a multinomial regression analysis.

To assess the impact of surgeon experience on the trifecta achievement rate, we divided our cases based on surgeon experience into three groups comprising of first 40 cases, 41–80 cases, and >80 cases.

Data analysis

Data were computed and analyzed using SPSS version 22 (IBM Corporation, Armonk, New York, U.S.A). For all statistical analyses, a two-sided $P < 0.05$ was considered statistically significant. To evaluate the impact of surgeon experience on perioperative outcomes, the patients were classified into 6 subgroups, including 20 consecutive cases.

For normally distributed data in the above-mentioned groups, the means of the various subgroups were compared using the one-way ANOVA followed by *post hoc* multiple comparisons test. The correlation was assessed using Pearson correlation coefficient for linear relationship between variables and Spearman's rho for nonlinear relationship between variables. Following a demonstration of correlation, the LCs was plotted for WIT, operative time and blood loss using polynomial regression analysis.

RESULTS

The preoperative clinical data of all 108 patients are summarized in Table 1. The mean tumor size was 3.7 ± 1.3 cms. 51.9% of the tumors were midpole tumors, while the remaining 48.1% were polar tumors [Table 2].

Table 1: Clinical characteristics of patients who underwent robotic partial nephrectomy in the study

Clinical characteristic	Result
Number of patients	108
Mean age, year (range)	53.5 (27–83)
Gender, *n* (%)	
Male	83 (76.9)
Female	25 (23.1)
Site, *n* (%)	
Left	62 (57.4)
Right	46 (42.6)
Co-morbidities, *n* (%)	
Diabetes mellitus	30 (27.8)
Hypertension	41 (38)
Chronic kidney disease	2 (1.9)
Ischemic heart disease	4 (3.7)
BMI, mg/kg/m^2 (range)	30.3 (18–45)
Previous abdominal surgery, *n* (%)	26 (24.1)
Mean tumor size, cm (range)	3.7±1.3 (1.3–8)
Polar location, *n* (%)	
Upper pole	22 (20.4)
Midpole	56 (51.9)
Lower pole	26 (24.1)
Mean warm ischemia time, min (range)	21.3±4 (14-34)
Mean operative time, min (range)	128.9±46.7 (90-325)
Mean console time, min (range)	62.9±7.7 (50-100)
Mean blood loss, ml (range)	124.4±40.8 (50-300)
Calyceal repair, *n* (%)	65 (60.2)
Length of stay, days, mean±SD (range)	3.9±1.6 (2–15)
Requirement of postoperative ICU care, *n* (%)	3 (2.8)

BMI=Body mass index, SD=Standard deviation, ICU=Intensive Care Unit

Table 2: Nephrometry scores, histopathology, and details of complications in patients evaluated in the study

Parameters	*n* (%)	
Renal score		
Low (4-6)	66 (61.1)	
Medium (7-9)	38 (35.2)	
High (10-12)	4 (3.7)	
PADUA score		
Low (6-7)	38 (35.2)	
Medium (8-9)	53 (49.1)	
High (≥10)	21 (19.4)	
T stage		
T1a	57 (52.8)	
T1b	47 (43.5)	
T2	3 (2.8)	
T3a	1 (0.9)	
Histopathology	***n* (%)**	**Positive surgical margins, *n* (%)**
Clear cell RCC	83 (76.9)	Surgical margins were negative in all 108 patients evaluated in the study
Papillary RCC	14 (13)	
Chromophobe RCC	7 (6.5)	
Mucinous and spindle cell tumor	1 (0.9)	
Angiomyolipoma	1 (0.9)	
Oncocytoma	1 (0.9)	
Renal cyst	1 (0.9)	
Complications	***n*=24**	**Details**
Total patients	20 (18.5)	
Clavien 1	4 (16.7)	Urine leak (1) prolonged ileus (3)
Clavien 2	15 (62.5)	Urine leak (1) transfusion (14)
Clavien 3	4 (16.7)	Ureteroureterostomy (1) angioembolization (3)
Clavien 4	1 (4.2)	Dialysis and ICU care (1)

PADUA=Preoperative aspects and dimensions used for anatomical, RCC=Renal cell carcinoma

With regard to intraoperative parameters, mean WIT was 21.3 ± 4 (range: 14–34); the mean operative time was 128.9 ± 46.7 (range: 90–325); the mean console time was 62.9 ± 7.7 (50–100); and the mean blood loss was 124.4 ± 40.8 (50–300). The mean preoperative serum creatinine and eGFR were 0.89 ± 0.21 mg/dL and 89.2 ± 18.5 ml/min per 1.73 m^2, respectively.

The details of the complications encountered and the histopathology are summarized in Table 2. None of our patients had positive surgical margins. Overall 18.5% of patients developed perioperative complications. The complications have been graded according to the modified Clavien system [Table 2].

According to the final histopathological examination, 43.5% of the tumors were classified as T1b while 2.8% of the tumors were classified as T2. The mean tumor size in this group was 4.6 cm (range: 4–6). One patient had renal sinus involvement which was classified as T3a. The mean RENAL score was 6.17 ± 1.4 (median interquartile range [IQR]: 6 (4–10]). The mean PADUA score was 8.24 ± 1.4 (median [IQR]: 8 [6–12]) [Table 2].

Impact of surgeon experience on perioperative parameters

Surgeon experience was found to correlate with WIT, operative time and blood loss ($P < 0.001$). Specifically, the median WIT was 20 min after the first 20 cases, the median operative time was <120 min after the first 20 cases and median blood loss was 100 ml after the first 20 cases [Figure 1].

Figure 1d demonstrates a reduction in the complication rate with increasing surgeon experience ($P < 0.001$). Specifically, only two complications were encountered in the last 48 cases. In contrast, out of the total of 24 complications, we encountered as many as 13 (54.2%) complications during the first 20 cases.

Analysis of learning curves

LC objectives were defined as WIT <20 min, operative time <120 min and blood loss <100 ml. We used polynomial regression analysis to estimate LCs for WIT, operative time and blood loss as these parameters were found to correlate with increasing surgeon experience as previously described [Figure 1]. LC plots are shown in Figure 2. The LC was 44 cases for WIT <20 min, 44 cases for operative time <120 min, and 54 cases for blood loss <100 ml [Figure 2].

Analysis of trifecta outcome

As previously described[19] trifecta outcome in RAPN was defined as WIT of ≤25 min, negative surgical margins and no perioperative complications. Trifecta outcome was achieved in 73 (67.6%) patients. Trifecta outcome improved with surgeon experience. In the initial phase of our LC that is the first 40 cases (case 1–40) trifecta was achieved in only 17 (42.5%) patients. In the next 40 cases (case 41–80), trifecta was achieved in 32 (80%) patients. Trifecta improved to 85.7% in the last 28 cases (case 81–108). Trifecta outcome

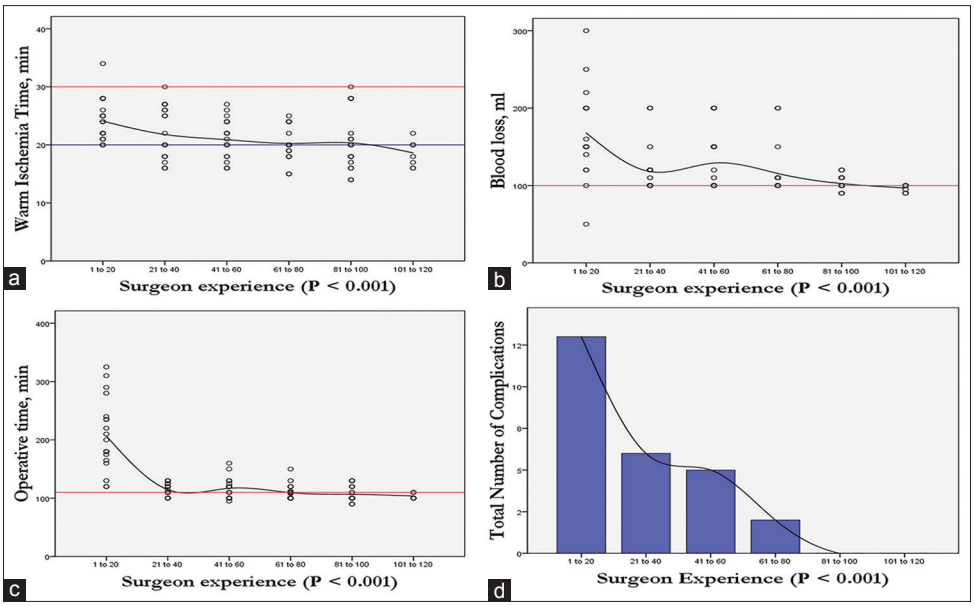

Figure 1: (a) Warm ischemia time according to surgeon experience. The red line indicates the 30-min time limit. The blue line indicates the 20-min time limit. (b) Blood loss according to surgeon experience. The red line indicates the median value. (c) Operative time according to surgeon experience. The red line indicates median value. (d) Total number of complications according to surgeon experience. The black line connects the mean values across the groups

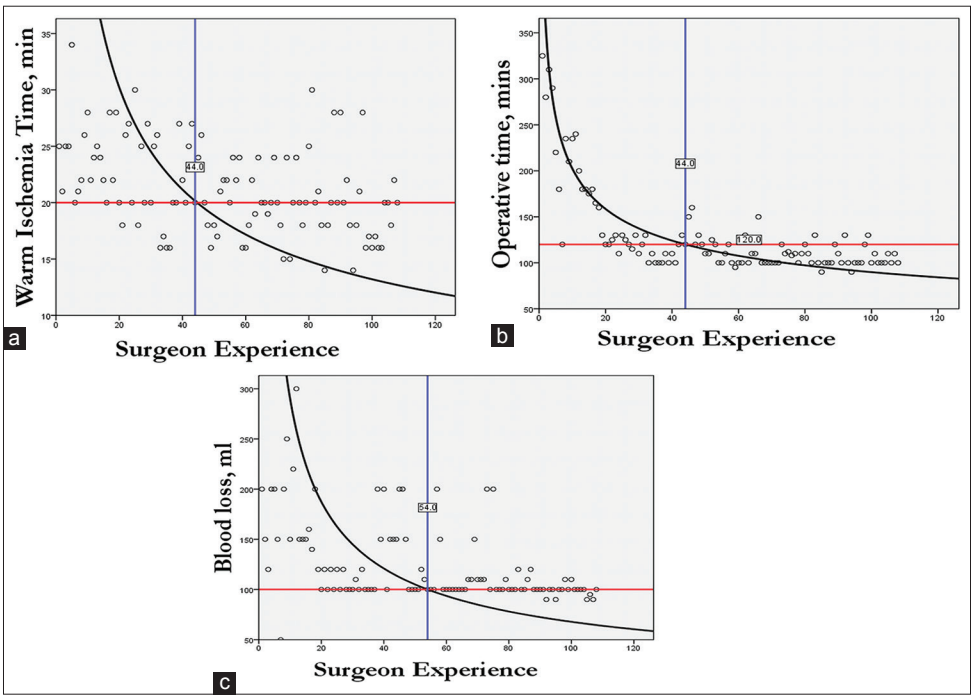

Figure 2: (a-c) Learning curves for warm ischemia time, operative time and blood loss plotted using polynomial regression analysis. The red line indicates the target parameter and the blue line corresponds to the number of cases to achieve the target. Based on the curves, the learning curve for warm ischemia time and operative time was found to be 44 cases and for blood loss, 54 cases

was found to correlate with surgeon experience ($P < 0.001$) in our study. The Pearson coefficient of correlation for this correlation was 0.432 [Table 3].

DISCUSSION

The present study demonstrated that for a surgeon with prior experience in LPN, RAPN is a safe, efficacious, minimally invasive procedure with a relatively short LC to achieve acceptable results in terms of WIT, operative time, blood loss, and complication rates. Our study shows that in the hands of an experienced, trained laparoscopic surgeon, RAPN can be started in the initial phase of the robotic LC without jeopardizing patient outcome. A similar study by Mottrie *et al*.[20] concluded that RAPN is a safe procedure with a short LC for surgeons who are experts in other

robotic procedures. They further added that during the LC period, excellent results in terms of WIT, console time, blood loss, and overall complications can be reached after about 30 cases. The present study demonstrated an LC of 44 cases [Figure 2]. However, in this study, the surgeon was new to robotic procedures and was in the initial phases of the LC during the transition from laparoscopic to robotic partial nephrectomy. Another interesting feature of our study is the number of T1b tumors (47 out of 108). This is due to the fact that with increasing experience we were able to confidently tackle more complex tumors using the robotic approach. This however may have contributed to increased WITs. Considering that there are no standard definitions of LC available, it is difficult to identify ideal parameters to evaluate the initial experience with a new surgical procedure. For partial nephrectomy, the WIT has been considered a crucial parameter for evaluating results and safety of any approach. Porpiglia *et al*. demonstrated that kidney damage occurs during LPN when warm ischemia is >30 min.[21] Subsequently, Thompson *et al*.[22] suggested that every minute counts when the renal hilum is clamped. Meta-analyses by Rod *et al*.[23] concluded that there is no evidence to support that limited WIT of <25 min has a higher risk of reducing renal function after partial nephrectomy. Our study however considered the strictest criteria proposed by Becker *et al*.[24] wherein he highlighted that WIT should be <20 min. In the present study, considering a cutoff value of <25 min for WIT would bring down our LC to 29 cases.

Recently, Veeratterapillay *et al*.[25] described their experience of RAPN in a large multicenter study done in the UK. They achieved "trifecta" outcomes in 68.4% of patients overall. The improvement of trifecta with increasing surgeon experience was highlighted in this study. They concluded that even though each center performs fewer than 50 RAPN cases per year, with the correct expertise outcomes compare well with the large published single-center series. In this study, we divided the cases into groups of 40 cases based on surgeon experience. This division was based on our LC of 44 cases. A study by Paulucci *et al*.[26] evaluated trends in perioperative outcomes of 250 consecutive cases beyond the initial LC of RAPN among multiple surgeons. They concluded that although RAPN can consistently be performed safely with acceptable outcomes after a small number of cases, improvement in trifecta achievement, WIT, EBL, blood transfusions and a shorter hospitalization continues to occur up to 300 procedures. We observed a similar trend in our cases with continuing improvement in trifecta achievement beyond the LC. Table 4 compares our data to these and other RAPN series described in literature. The literature review shows the high percentage of T1b tumors in our series. Another important aspect is the zero positive margin rates in our study. Taken together our data show that even larger T1b tumors can be tackled safely during the LC of RAPN.

Table 3: Trifecta achievement following robot-assisted partial nephrectomy

Surgeon experience	1-40 cases, *n* (%)	41-80 cases, *n* (%)	>80 cases, *n* (%)
Warm ischemia time			
<20 min	14 (35)	24 (60)	20 (71.4)
<25 min	29 (72.5)	36 (90)	24 (85.7)
Complications	14 (35)	6 (15)	0 (0)
Positive surgical margins	Nil	Nil	Nil
Trifecta*	17 (42.5)	32 (80)	24 (85.7)

*Trifecta outcome was found to correlate with surgeon experience. Pearson's coefficient of correlation 0.432 ($P<0.001$)

Another important parameter for evaluating the safety of a surgical procedure is the complication rate. Our complication rate was 18.5% which is within the range reported for most RAPN and LPN series.[25-29] We classified our complications according to the modified Clavien system and found that only 20.9% of the total number of complications were Clavien 3 or above. 54.2% of our complications were encountered during the first 20 cases, and hence, we advocate mentorship during the initial phase of the LC to achieve optimal results. Concerning the operative time, console time, and EBL, our results are well within the ranges previously reported in literature.[25-29]

CONCLUSION

The study demonstrates that for a surgeon trained in laparoscopy, RAPN is a safe procedure that can be attempted at an initial phase of the robotic LC and excellent

Table 4: Robot-assisted partial nephrectomy: Review of literature

Study	Study size (*n*)	Mean tumor size (cm)	Median WIT (min)	T1b tumors (%)	PSM (%)	Median blood loss (ml)	Median operative time (min)	Complication rate (%)	Trifecta (%)
Veeratterapillay *et al*.	250	3	16.7	NR	7.3	204	141	16.4	68.4
Paulucci *et al*.	960	3	16	20.4	4	100	179	12	72.2
Andrade *et al*.	115	2.6	20	16	1.7	200	180	24	53.9
Lista *et al*.	339	3	17	13.3	6.5	100	130	14.5	67
Ploussard *et al*.	65	3.9	21	40	7.7	150	183	24.6	56.9
Kaouk *et al*.	400	3.17	19	19.7	2.25	200	180	15.3	NR
Dube *et al*.	171	2.9	19	NR	NR	217	214	5.9	NR
Our study	108	3.7	20	43.5	0	100	110	18.5	67.6

PSM=Positive surgical margin, NR=Not Reported, WIT=Warm ischemia time

results in terms of WIT, operative time, blood loss, overall complications, and margin status can be reached after about 44 cases. Surgeon experience in crucial for "trifecta" achievement following RAPN.

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