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ORIGINAL ARTICLE

A multi-institutional report of peri-operative and functional outcomes after robot-assisted partial nephrectomy in patients with a solitary kidney

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Abstract

To evaluate peri- and post-operative outcomes after robotic partial nephrectomy (RPN) in patients with a solitary kidney. A multi-institutional database of 1868 patients was used to identify 35 patients with a solitary kidney who underwent RPN at six different centers from 2007 to 2016. Peri-operative outcomes were summarized with descriptive statistics. We assessed the change in eGFR over time with a linear mixed-effects model. Median operative time, ischemia time, and estimated blood loss were 172 min, 16 min, and 113 mL, respectively. There were no positive surgical margins. The median length of stay was 1 day (range 1–7), and over half (54.3%) of patients were discharged one post-operative day 1. Seven post-operative complications occurred in six patients (17.1%); of which four were Clavien I, two were Clavien II, and one was Clavien III. The linear decline in eGFR up to 24 month post-RPN was marginal and not significant (ß = − 0.14; 95% CI = − 0.51, 0.23; $p = 0.453$), with predicted mean eGFR decreasing from 59.2 to 55.8 mL/min/1.73 m^2 at 24 months. These results suggest that, in patients with a solitary kidney, RPN is a safe and feasible treatment option. In patients with a solitary kidney, RPN did not significantly compromise renal function for up to 2 years after surgery.

Keywords Renal cancer · Nephron sparing surgery · Solitary kidney · Glomerular filtration rate · Partial nephrectomy · Robotics

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Introduction

A mass suspicious for malignancy in a solitary kidney is considered an indication for nephron sparing surgery (NSS) whenever feasible [1, 2]. Partial nephrectomy (PN) is the preferred method of NSS, because it can prevent or delay the need for renal replacement therapy and offers good oncologic control [1, 2].

In the setting of a solitary kidney, the preservation of renal function is increasingly important. There have been only a handful of studies examining the outcomes after robotic partial nephrectomy (RPN) in patients with a solitary kidney [3–5]. These studies found that RPN was safe and effective, did not significantly compromise renal function in the peri-operative period, and was associated with short warm ischemia times (WIT). Although encouraging, these findings were limited by short follow-up periods. Therefore, we evaluated outcomes after RPN, in patients with a solitary kidney, for up to 2 years after surgery.

Materials and methods

Data source

A multi-institutional database of 1868 patients was used to identify 35 patients with a solitary kidney who underwent RPN at six different United States centers. Surgeries were performed by one of six experienced robotic surgeons, between 2007 and 2016. Data were maintained in an online, IRB-approved database (REDCap) [6].

Study variables and statistics

Evaluated clinical and demographic characteristics included gender, body mass index (BMI), Charlson comorbidity index (CCI), baseline estimated glomerular filtration rate (eGFR), baseline chronic kidney disease (CKD) stage, tumor location, clinical tumor size and stage, and RENAL nephrometry score.

Intra-operative variables included operative time, console time, operative approach, WIT, clamping technique, estimated blood loss (EBL), collecting system injury, number of tumors removed, incidence of intra-operative complications, and surgical margin status.

Post-operative variables included length of stay (LOS), complications, and eGFR. Complications were graded according to the Clavien–Dindo system [7]. Significant complications were defined as grade III or higher.

Continuous variables were represented by the median and inter-quartile ranges. Categorical variables were presented as percentages or proportions. We assessed the change in eGFR over time using a linear mixed-effects model with a random intercept only. Follow-up time, for patients included in the analysis, ranged from 2 to 24 months. A loess plot was generated to visually represent changes in eGFR over time. A comparison of average eGFR at 4–12 months for patients undergoing selective arterial clamping and those undergoing total hilar clamping was performed using Welch's t test.

Results

Demographic and clinical characteristics

Median age was 64 years and 74.3% ($n=26$) of the patients were male. Median BMI was 28.7 and 48.6% of the patients ($n=17$) had a CCI of two or higher. Median tumor size was 2.4 cm (range 1.1–7.9 cm). Median RENAL nephrometry score was 6. 45.1% of patients had a moderate or high complexity tumor, 14.3% had a tumor abutting the renal hilum, and 12.9% had a completely endophytic tumor. Additional patient and tumor characteristics can be found in Table 1.

Intra-operative and post-operative outcome

Median operative time was 172 min (range 105–481 min), including 135 min of console time (range 65–360 min). 30 of the cases (85%) were transperitoneal. The median WIT was 16 min (range 8–32 min). The clamping techniques utilized were main artery clamping +/− renal vein clamping ($n=17$, 50.0%), selective arterial clamping ($n=13$, 38.2%), or off-clamp technique ($n=4$, 11.8%). Median EBL was 113 mL (range 25–1600 mL). Two patients had more than one tumor removed during the case. Only one patient experienced an intra-operative complication, which was a bowel injury. There were no positive surgical margins (PSM).

The median LOS was 1 day (range 1–7) with over half (54.3%) of patients discharged on post-operative day 1. There were seven post-operative complications in six patients (17.1%). The distribution by Clavien grade was four grade I complications, two grade II complications, and one grade III complication. The only major post-operative complication was acute kidney injury requiring readmission and stent placement after surgery for a T2a renal mass (Table 2).

eGFR post-RPN

The median baseline eGFR was 59.2 mL/min/1.73 m^2 (range 32.6–88.8). Median follow-up time was 8 months (IQR: 1.5 weeks–24 months; range: 18 h–60 months). Preoperatively, 60% of patients had CKD stage 2 and 40% had CKD stage 3. Only patients with at least 2 months of follow-up were included in the linear fixed-effects model. Follow-up

Table 1 Patient and tumor characteristics

N	35
Age (years)	64 (53–70; 36–78)
Sex	
Female	9 (25.7%)
Male	26 (74.3%)
BMI	28.7 (25.4–36.8; 15.1–59.0)
Charlson Comorbidity Index	
0	12 (34.3%)
1	6 (17.1%)
2+	17 (48.6%)
Baseline eGFR	59.2 (53.0-70.1; 32.6–88.8)
Baseline CKD stage	
1	0 (0.0%)
2	21 (60.0%)
3	15 (40.0%)
4	0 (0.0%)
5	0 (0.0%)
Clinical tumor size	2.4 (2.1–3.5; 1.1–7.9)
Clinical tumor stage	
cT1a	28 (80.0%)
cT1b	5 (14.3%)
cT2a	2 (5.7%)
RENAL nephrometry score	6 (5–9; 4–11)
Low (4–6)	17 (54.8%)
Med (7–9)	10 (32.2%)
High (10–12)	4 (12.9%)
% Endophytic	
< 50%	7 (22.6%)
> 50%	20 (64.5%)
100%	4 (12.9%)
Hilar	4 (14.3%)
Tumor location	
Anterior	16 (55.2%)
Posterior	8 (27.6%)
Neither	5 (17.2%)
Histologic subtype	
Clear cell	20 (58.8%)
Papillary	6 (17.6%)
Chromophobe	3 (8.8%)
Oncocytoma	3 (8.8%)
Cystic RCC	1 (2.9%)
Benign cyst	1 (2.9%)

Percentages calculated out of those with complete data on the variable analyzed which is less than 35 patients for certain variables

For continuous variables, median presented with inter-quartile range; range in parenthesis. For categorical variables, frequencies presented with % in parenthesis

data from 2 to 24 months post-RPN were available in 15 (42.9%) patients. The linear term for eGFR decline over time, as calculated from the mixed-effects model, was not statistically significant ($\beta = -0.14$; 95% CI = −0.51, 0.23; $p = 0.453$) indicating negligible eGFR decline at up to 24 months post-RPN. Predicted mean eGFR decreased from 59.2 to 55.8 at 24 months ($\Delta = -3.4$ mL/min/1.73 m^2) (Table 3). Figure 1 provides a graphical representation of the change in eGFR over time in patients with a solitary kidney.

A sub-analysis was performed to compare the change in eGFR among patients who underwent renal artery and selective arterial clamping. Patients who underwent off-clamp RPN were excluded, because the eGFR was available for only one patient. The eGFR at baseline was not significantly different between patients who underwent renal ($n = 17$) artery and selective artery clamping ($n = 16$). Estimated GFR was compared a 4–12 months and at greater than 12 months (renal artery clamping $n = 8$; selective arterial clamping $n = 4$). If a patient had two eGFRs during one time period, the eGFRs were averaged together. At both 4–12 months and at greater than 12 months, there was no significant difference in eGFR between patients who underwent renal artery or selective arterial clamping.

Table 2 Intra-operative and post-operative outcomes

Operative time (min)	172 (147–224; 105–481)
Robotic time (min)	135 (101–183; 65–360)
Ischemia time (min)	16 (11–21; 8–32)
Estimated blood loss (mL)	113 (100–275; 25–1600)
Positive surgical margins	0 (0.0%)
Collecting system entry	17 (53.1%)
Clamp technique	
Main artery	17 (50.0%)
Selective arterial	13 (38.2%)
Off-clamp	4 (11.8%)
2 + tumor removed	2 (5.9%)
Length of stay (days)	1 (1–2; 1–7)
1	19 (54.3%)
2	8 (22.9%)
3+	8 (22.9%)
Post-operative complication	7 (17.1%)

Percentages calculated out of those with complete data on the variable analyzed which is less than 35 patients for certain variables

For continuous variables, median presented with inter-quartile range; range in parenthesis. For categorical variables, frequencies presented with % in parenthesis

Table 3 Predicted eGFR Following RPN

	Pre-RPN	6 months	12 months	18 months	24 months
Predicted eGFR	59.2	58.3	57.5	56.7	55.8

Predicted eGFR was derived from the univariable linear mixed-effects model. Term for linear decline not statistically significant ($\beta = -0.14$; 95% CI = −0.51, 0.23; $p = 0.453$)

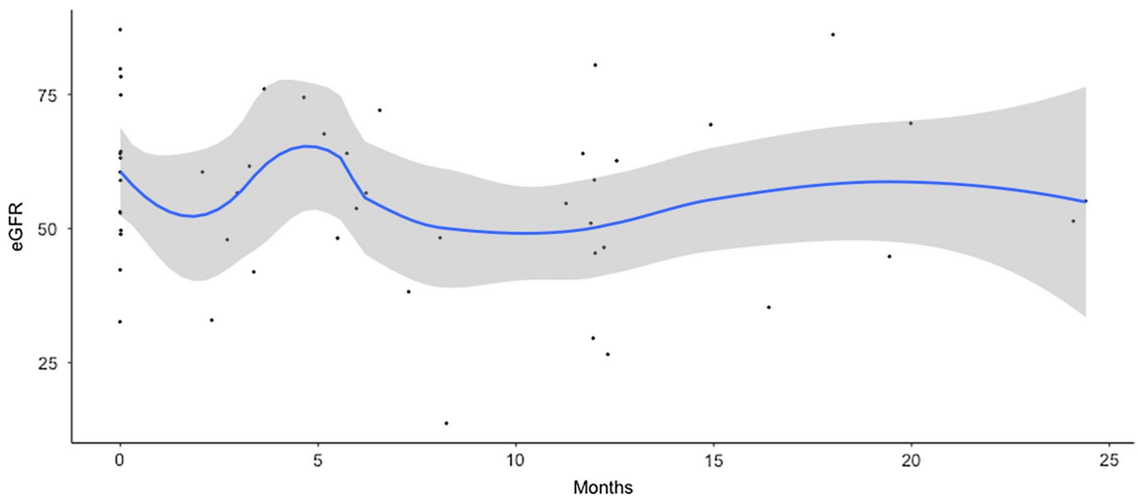

Fig. 1 Locally weighted smoothing (LOESS) plot of eGFR over time in patients with a solitary kidney after RPN. Each dot represents a single patient's eGFR (*Y* axis) at various time points after surgery (*X* axis). The fitted LOESS curve is in blue. The 95% confidence interval is represented by the grey area

Comments

In patients with a solitary kidney, preservation of renal function is paramount and depends directly on surgical outcomes. As the popularity of minimally invasive surgical techniques has increased, so too has the application of these techniques to more complicated patients, such as those with a solitary kidney. Currently, robotic surgery is the dominant minimally invasive approach [1]. There have been four previous reports of RPN in a solitary kidney [3–5, 8], three of these are from either the same multi-institutional database [3, 5] or from a single institution's subset of patients from this database [4]. A comparison of our results with these studies can be found in Table 4.

All of these studies reported short-term renal functional outcomes. Hillyer et al. [3] found that, at 6 months, there was no significant change in eGFR after RPN. This is the only other study that compared post-operative function to pre-operative function. Panumatrassamee et al. also evaluated eGFR at 6 month post-operatively and found that the average eGFR decreased from 50 mL/min/1.73 m^2 to 38 mL/min/1.73 m^2 [4]. Zagar et al. divided their 40-patient cohort into those with simple or complex renal masses according to RENAL nephrometry score. They found that, in each group, 82% and 80% of eGFR was preserved at "beyond 3 months" and at a median follow-up of 6 months, respectively [5]. Most recently, Arora et al. [8] found that aGFR decreased by 8 mL/min/1.73 m^2 at 3 months post-operatively.

The present study compares baseline renal function to renal function at 2 year post-operatively. Although the optimal duration of follow-up is unknown, it is well established that renal function fluctuates after PN. Typically, eGFR initially declines sharply, but then improves as the remaining kidney parenchyma undergoes a compensatory hypertrophy [9]. Ghoneim et al. reported that renal function stabilizes as early as 1 month after surgery [10], whereas Saranchuk et al. [11] found that renal function stabilizes between the first year and second year after PN. In addition, for most patients who do develop CKD, these changes take several months to occur. Adkins et al. found a significant increase in the average serum creatinine 2 years after PN in a solitary kidney [12], and Fergany et al. found that among patients with a solitary kidney who develop CKD after PN; the minimum time to progression was 1 year [13]. Therefore, we believe that assessing function at 2 year post-operatively is a more accurate assessment of the effects of RPN on renal function.

Three other findings from this study are worth further mention. First, no positive surgical margins (PSM) were identified. The previous studies reported PSM rates that ranged from 3.8–10% [3–5, 8]. These rates are higher than those reported for RPN in patients with a normal contralateral kidney [14, 15]. Arora et al. hypothesized that the higher PSM rates were secondary to the surgeons' attempt to maximize renal preservation [8]. Our results suggest that it is possible to preserve renal function without sacrificing oncologic efficacy.

Second, the average hospital stay among our patients was 1 day, compared to the 3 days previously reported in the studies of RPN in patients with a solitary kidney [3–5]. Shorter hospital stays are important, because they have been associated with greater patient satisfaction and lower costs [16]. We believe that, even in this high-risk subset of patients, short hospital stays are possible.

Finally, consistent with the four aforementioned studies, which reported WIT of 15.5–22 min [3–5, 8], our median WIT was 16 min. Although the importance of short ischemia

Table 4 Comparison of the current literature on robotic partial nephrectomies

	Present study ($n=35$)	Arora et al. [8] ($n=74$)	Zargar et al. [5] RENAL 4–8 ($n=30$)	Zargar et al. [5] RENAL 9–12 ($n=10$)	Panumatrassamee et al. [4] 9 ($n=15$)	Hilyer et al. ($n=26$)
Size, median (IQR)	2.7 (2-3.8)	2.3 (1.8–3.7)	2.5 (2.35)	4.5 (2.9)	3.2 (2.5–5.3)	4.3 (2.9-5)
RENAL score, median (IQR)	6 (5–9)	6 (5–9)	6 (2)	9.5 (1)		
Low (4–6) *n* (%)	17 (55)	34 (46)			8 (53)	11 (42)
Med (7–9) *n* (%)	10 (32)	27 (36)			4 (27)	7 (27)
High (10–12) *n* (%)	4 (13)	5 (8)			3 (20)	3 (12)
EBL, mL median (IQR)	113 (100–275)	150 (100–350)	200 (300)	225 (288)	150 (100–300)	225 (100–437)
WIT, min median (IQR)	16 (11–21)	15.5 (8.75-20)	15 (9)	22.7(5.8)*	15 (0–24)	17 (12–28)
All complications, *n* (%)	7 (17)	18 (24)	9 (30)	4 (40)	5 (33)	3 (11.5%)
Positive surgical margins, *n* (%)	0 (0)	4 (5.4)	2(6.7)	1 (10)		1 (3.8)
Hospital stay, days median (IQR)	1 (1–2)		3 (5)	4 (1.5)	3 (3–4)	3 (2–4)
Preop eGFR	61 (53–70)	61 (50–72)			50 (42–63)	59 (44–73)
Post-op eGFR	56	53 (35–62)			38	44 (37–59)
% Preservation of eGFR, median (IQR)			82 (23)	80 (24)		
Time from preop eGFR to post-op	2 years	3 months	Beyond 3 months	6 months (24)	6 months	6 (5–9.7)
Significant change in eGFR	No					No

times for the preservation of renal function remains a topic of debate [17, 18], it is generally accepted that a WIT of less than 25 min is desirable, and that additional decreases in WIT may provide further benefit for the preservation of renal function [18–20]. It is important to note that, on average, patients in these studies had small, low complexity tumors. The 22 min WIT is from Zagar et al's experience with RPN for high complexity tumors, which had nephrometry scores that ranged 9–12 [5]. These results are consistent with the previous studies, which found that that longer WIT are associated with higher complexity tumors [21, 22].

Limitations of this study include its retrospective design, small sample size, and variability in follow-up. These limitations are in part due to the low incidence of RPN in solitary kidneys. More specifically, checking the creatinine at pre-specified time points, and accounting for factors such as residual renal mass after PRN and subsequent renal hypertrophy would have made our results more robust. Similarly, actually measuring GFR by technetium-99m-diethylene-triaminepentaacetic acid (Tc-99m DTPA) scan could have confirmed the accuracy of our results. However, since this was a multi-institutional, retrospective analysis, available data and follow-up intervals were variable and surgeon dependent. In addition, we used eGFR to evaluate renal function throughout the study period. While our study has continued to expand our understanding of RPN use in solitary kidneys, more definitive conclusions would have to come from randomized trials that compare surgical and oncologic outcomes after open, laparoscopic, and robotic PN in patients with a solitary kidney.

Conclusion

In patients with a solitary kidney, RPN is a feasible and safe treatment option that does not significantly compromise oncologic outcomes or renal function. Our results suggest that patients with a solitary kidney who undergo an RPN do not experience a decrease in renal function for up to 2 year post-operatively.

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Compliance with ethical standards

Conflict of interest Ronney Abaza has received research funding from Conmed Inc. and educational program funding from Intuitive Surgical. James Porter has received research support from Ceerva, is on the advisory board for C-SATS, and is a speaker for Intuitive Surgical. Zeynep Gul, Kyle Blum, David Paulucci, Daniel Eun, Akshay Bhandari, Ashok Hemal, and Ketan Badani have no conflicts of interest to report.

Informed consent Informed consent was obtained from all individual participants included in this study.

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