Original Article

Perioperative outcomes following robot-assisted partial nephrectomy for complex renal masses: A Vattikuti Collective Quality Initiative database study

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ABSTRACT

Introduction: Outcomes of robot-assisted partial nephrectomy (RAPN) depend on tumor complexity, surgeon experience and patient profile among other variables. We aimed to study the perioperative outcomes of RAPN for patients with complex renal masses using the Vattikuti Collective Quality Initiative (VCQI) database that allowed evaluation of multinational data.

Methods: From the VCQI, we extracted data for all the patients who underwent RAPN with preoperative aspects and dimensions used for an anatomical (PADUA) score of ≥10. Multivariate logistic regression was conducted to ascertain predictors of trifecta (absence of complications, negative surgical margins, and warm ischemia times [WIT] <25 min or zero ischemia) outcomes.

Results: Of 3,801 patients, 514 with PADUA scores ≥10 were included. The median operative time, WIT, and blood loss were 173 (range 45–546) min, 21 (range 0–55) min, and 150 (range 50–3500) ml, respectively. Intraoperative complications and blood transfusions were reported in 2.1% and 6%, respectively. In 8.8% of the patients, postoperative complications

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were noted, and surgical margins were positive in 10.3% of the patients. Trifecta could be achieved in 60.7% of patients. Clinical tumor size, duration of surgery, WIT, and complication rates were significantly higher in the group with a high (12 or 13) PADUA score while the trifecta was significantly lower in this group (48.4%). On multivariate analysis, surgical approach (retroperitoneal vs. transperitoneal) and high PADUA score (12/13) were identified as predictors of the trifecta outcomes.
Conclusion: RAPN may be a reasonable surgical option for patients with complex renal masses with acceptable perioperative outcomes.

INTRODUCTION

Partial nephrectomy (PN) has become the standard of care for treating small renal masses due to its superior functional and equivalent oncological outcomes.[1] Dissemination of robotic technology has made PN feasible for many complex tumors.[2,3] Outcomes following PN may be impacted by the surgeon, patient, and tumor-related factors. Multiple comprehensive tumor-related and patient-related outcome measures have been reported in the literature.[1] These outcome measures have been well correlated with perioperative outcomes. Radius, endophytic/exophytic, nearness, anterior/posterior location (RENAL), and Preoperative aspects and dimensions used for an anatomical classification (PADUA) nephrometry scores are the two most commonly used parameters for preoperative assessment of tumor complexity.[4,5] These scores correlate well with perioperative outcomes such as complications and warm ischemia time (WIT) following PN.[5-8]

Recently, multiple observational studies have reported outcomes of robot-assisted PN (RAPN) to manage complex renal masses. However, most of these studies have a limited number of patients and are based on single-center experience. The multinational Vattikuti Collective Quality Initiative (VCQI) database provides an excellent opportunity for studying perioperative outcomes following RAPN for complex renal masses. Furthermore, different learning curve stages for the surgeons at the participating institutions could represent the real-world scenario in managing complex renal masses. Therefore, this study aimed to report perioperative outcomes following RAPN in patients with complex renal masses (PADUA score ≥10). The secondary objective of this study was to identify predictors of trifecta in patients with complex renal masses.

MATERIALS AND METHODS

Vattikuti Collective Quality Initiative database

VCQI is a prospective web-based multi-institutional collaborative database. Data for RAPN are contributed by 18 participating institutions from 9 countries (the United States, the United Kingdom, India, Italy, Portugal, Belgium, Turkey, Australia, and South Korea). The database is Health Insurance Portability and Accountability Act compliant and ethics clearance was obtained from each participating institution. For this study, we extracted data for all the patients who underwent RAPN for renal masses with a PADUA score of ≥10. Patients with low or moderate complexity tumors were excluded from the analysis. Data for various demographic, operative, pathological, and postoperative outcomes were extracted for descriptive analysis.

Baseline data included age, sex (male/female), body mass index (BMI), clinical tumor size, and estimated glomerular filtration rate (eGFR) using modified diet in renal disease equation. Clinical data pertaining to symptoms (absent/local/systemic), location of the tumor (upper/middle/lower pole), number of tumors (single/multiple), solitary kidney, and PADUA risk scores were obtained. Operative factors included surgical access (retroperitoneal/transperitoneal), operative time, WIT, blood loss, intraoperative blood transfusion, need for conversion to radical nephrectomy or open surgery, and intraoperative complications. Postoperative complications were graded as per Clavien–Dindo classification up to 30 days following surgery. Trifecta was defined as the absence of complications, negative surgical margins, and WIT <25 min or zero ischemia.[9]

Statistical analysis

Descriptive analysis was performed for all the perioperative variables. To compare PADUA score groups, "Kruskal–Wallis" and "Pearson Chi-square" tests were used for continuous and categorical variables, respectively. Multivariate logistic regression was used to identify predictors of trifecta outcomes. All the statistical analyses were conducted using SPSS version 23 (IBM corporation, New York, USA) and performed with a significance level $P < 0.05$.

RESULTS

Data for patients who underwent RAPN between October 2014 and March 2020 at various participating institutions were extracted from the database. Of 2,550 patients with complete data 514 patients with PADUA scores ≥10 were included in this study. The median age was 56 years, and there were 340 (66%) males and 174 females (34%). Mean clinical tumor size and BMI were 43 mm and 26.8 kg/m^2, respectively. The median Charlson Comorbidity Index score was 1 and range 0–7. Most of the patients had incidental detection of renal mass (76.8%); only 21% and 2.1% of the patients had local or systemic symptoms, respectively. Further data on tumor side, location, face, and laterality are

provided in Table 1. The median preoperative hemoglobin, serum creatinine, and eGFR were 14 g/dL, 0.9 mg/dL, and 80.5 ml/min, respectively. The median PADUA risk score was 10 and further distribution according to PADUA scores is provided in Table 1.

Most of the patients had a single renal mass (97.7%) and underwent transperitoneal RAPN (82.9%). Selective arterial clamping and off-clamp surgeries were performed in 13.8% and 4.9% of the patients, respectively. The median duration of surgery and WIT was 173 min and 21 min, respectively. WIT was >25 min in 138 patients (26.8%). Median blood loss was 150 ml, and 2.1% required intraoperative blood transfusion. Intraoperative complications were noted in 6% of the patients. The most common intraoperative complication was "Gross violation of tumor bed" (inadvertent dissection into the tumor during surgery) (15 patients) followed by bleeding from the tumor bed (7 patients). The conversion to open surgery or radical nephrectomy was needed in 1 and 14 patients, respectively. The median length of stay was 3 days. Postoperative complications were noted in 8.8% of the patients. Most of these complications were minor (Grade I and II), and only 2.1% of the patients had major complications [Table 1].

On final histopathological analysis, 13% and 87% of the patients had benign and malignant tumors, respectively.

Table 1: Baseline data of the patients included in this study (*n*=514)

Variable	*n* (%)
Age (years), median (range)	56 (16-87)
Sex (male/female)	340/174
BMI (kg/m^2), mean±SD	26.8±5.5
Tumor size (mm), mean±SD	43±17.6
CCI, median (range)	1 (0-7)
Clinical symptoms	
Asymptomatic	395 (76.8)
Local	108 (21.1)
Systemic	11 (2.1)
Single kidney	13 (2.5)
Bilateral tumor	14 (2.7)
Tumor side	
Right	238 (46.3)
Left	276 (53.7)
Face of tumor	
Anterior	265 (51.6)
Posterior	249 (48.4)
Polar location of tumor	
Upper	136 (26.5)
Mid	257 (50)
Lower	121 (23.5)
Preoperative hemoglobin (g/dL), median (range)	14 (7.5-19)
Preoperative creatinine (mg/dL), median (range)	0.9 (0.5-9.7)
Preoperative eGFR (ml/min), median (range)	80.5 (4-190)
Median PADUA risk score	
10	259 (50.4)
11	158 (30.7)
12	80 (15.6)
13	17 (3.3)
Number of lesions operated	
1	502 (97.7)
2	10 (1.2)
3	1 (0.2)
4	1 (0.2)

SD=Standard deviation, BMI=Body mass index, eGFR=Estimated glomerular filtration rate, CCI=Charlson Comorbidity Index, PADUA=Preoperative aspects and dimensions used for an anatomical

Table 2: Operative and pathological data of the patients included in this study (*n*=514)

Variable	*n* (%)
Surgical access	
Transperitoneal	426 (82.9)
Retroperitoneal	88 (17.1)
Selective arterial clamping	71 (13.8)
Off-clamp	25 (4.9)
Indocyanine green dye use	165 (32.1)
Outer renorrhaphy	442 (85.9)
Inner renorrhaphy	444 (86.3)
Pelvicalyceal system repair	267 (51.9)
Operative time (min), median (range)	173 (45-546)
WIT (min), median (range)	21 (0-55)
Blood loss (ml), median (range)	150 (50-3500)
Intraoperative transfusion	11 (2.1)
Intraoperative complications	31 (6)
Conversion to open	1
Gross violation of tumor bed	15
Injury to abdominal organs	1
Injury to major vessels	1
Major bleeding from tumor bed	7
Others	6
Need for conversion to radical nephrectomy	14 (2.7)
Length of stay (days), median (range)	3 (1-19)
Postoperative complications	45 (8.8)
Grade I	15 (2.9)
Grade II	19 (3.7)
Grade III	11 (2.1)
Grade IV	0
Pathology	
Benign	67 (13)
Malignant	446 (87)
Benign pathology	
Angiomyolipoma	20 (3.9)
Oncocytoma	31 (6)
Metanephric adenoma	1 (0.2)
Benign cysts	5 (1)
Others	10 (2)
Malignant pathology	
Clear cell	351 (68.3)
Papillary cell	50 (9.7)
Chromophobe	36 (7)
Others	10 (2)
Fuhrman nuclear grading (for clear cell)	
1	41 (11.6)
2	199 (56.6)
3	105 (29.9)
4	6 (1.7)
Positive margins	53/514 (10.3)
T stage (*n*=446)	
T1a	229 (44.6)
T1b	159 (30.9)
T2a	17 (3.3)
T2b	21 (4.1)
T3a	20 (3.9)
Trifecta	312 (60.7)

WIT=Warm ischemia time

The most common malignant histological subtype was clear cell carcinoma, whereas oncocytoma was the most common benign tumor. Fuhrman nuclear grading (for clear cell RCC) and T-stage are provided in Table 2. Surgical margins were positive in 10.3% of the patients. Patients who underwent transperitoneal RAPN had significantly higher positive margins than retroperitoneal RAPN (11.9% vs. 2.2%). Trifecta outcomes were attained in 60.7% of the patients. Trifecta outcomes were significantly higher in patients who underwent retroperitoneal RAPN (77.2% vs. 57.2%, $P = 0.000$).

Comparison of patients according to the PADUA score is provided in Table 3. Clinical tumor size, duration of surgery, WIT, and complication rates were significantly higher in the group with a high (12 or 13) PADUA score. There was no significant difference in the three groups for intraoperative complications, need for intraoperative blood transfusion, positive surgical margins, and WIT >20 min. Trifecta outcomes were significantly lower in high PADUA score group 12/13 (48.4%). On multivariate analysis, PADUA risk group and surgical approach (retroperitoneal vs. transperitoneal) were identified as an independent predictor of trifecta outcomes [Table 4].

DISCUSSION

PN has become a standard surgical option for treating small renal masses.[10,11] It has been noted to have equivalent oncological outcomes with acceptable morbidity.[2,10,12,13] Moreover, renal function preservation is superior to radical nephrectomy and this is associated with increased overall survival due to a decrease in other causes of mortality such as cardiovascular events.[6,14] Therefore, most incidentally detected renal masses are best removed through a nephron-sparing approach to preserve renal function. Excision of some of these renal masses may not be straightforward due to their size, location, or proximity to hilar vasculature. Open PN with cold ischemia would likely be the default option for many of these complex tumors. However, with the availability of robotic equipment and its numerous advantages such as better 3D vision, ergonomics, precision, Endowrist® and motion scaling, many complex renal masses can be removed minimally invasively. During the past decade, multiple retrospective single or multicenter studies have been published assessing the feasibility of RAPN for managing complex renal masses[7,15-27] [Table 5]. With this multi-institutional study, we report our results of RAPN in patients with complex renal masses (PADUA ≥10). To the best of our knowledge, the present study represents the most extensive experience of managing complex renal masses with the robot.

The median operative time of 173 min noted in the present study is well within the range of mean operative times indicated in the previous RAPN series for complex renal masses[3] [Table 5]. Median WIT also compares well to these previous studies [Table 5]. However, ischemia time is undoubtedly longer than previous RAPN studies reporting low-to-moderate complexity tumors.[15,23,24] A longer WIT was also the most common cause of failure to achieve a trifecta in the present study (26.8%). Longer WIT noted in the present study could be attributed to a more challenging dissection and reconstruction of the defect in tumors with high complexity. Tumor complexity, in fact, is a predictor of WIT.[7] WIT is also a proxy marker for renal

Table 3: Comparison of perioperative outcomes between the preoperative aspects and dimensions used for an anatomical score groups

Variable	PADUA score 10 (*n*=259), *n* (%)	PADUA score 11 (*n*=158), *n* (%)	PADUA score 12 and 13 (*n*=97), *n* (%)	*P*
Age, mean±SD	55.9±13.5	54.3±14.1	55±13.6	0.261$
BMI (kg/m^2), mean±SD	28.1±5.2	27.6±6	27.8±5.3	0.220$
Tumor size (mm), mean±SD	42±16.7	42.5±17.6	49.7±18.8	0.001$
Operative time, mean±SD	174±23.8	177±68.1	197±74.4	0.127$
WIT, mean±SD	20.9±8.5	20.3±8.4	23.8±9.2	0.023$
Blood loss (ml), mean±SD	214±271	216±203	350±471	0.000$
WIT >25 min	63 (24.3)	40 (25.3)	35 (36.08)	0.073*
Access				
Retroperitoneal	41 (15.8)	30 (19)	17 (17.5)	0.704*
Transperitoneal	218 (84.2)	128 (81)	80 (82.5)	
Intraoperative transfusion	5 (1.9)	3 (1.9)	3 (3.1)	0.772*
Intraoperative complication	15 (5.8)	11 (7)	5 (5.1)	0.819*
Need for conversion to radical nephrectomy	5 (1.9)	7 (4.4)	2 (2.06)	0.285*
Postoperative complications	21 (8.1)	9 (5.7)	15 (15.4)	0.024*
Grade I	8 (3.1)	4 (2.5)	3 (3.1)	0.048*
Grade II	8 (3.1)	4 (2.5)	7 (7.2)	
Grade III	5 (1.9)	1 (0.6)	5 (5.1)	
Grade IV	0	0	0	
Positive surgical margin	33 (12.7)	10 (6.3)	10 (10.3)	0.113*
Trifecta	158 (61)	107 (67.7)	47 (48.4)	0.009*

*Chi-square test, $Kruskal-Wallis test. SD=Standard deviation, BMI=Body mass index, PADUA=Preoperative aspects and dimensions used for an anatomical, WIT=Warm ischemia time

Table 4: Multivariate analysis to identify predictors of the trifecta

Trifecta	OR	Lower limit of CI	Upper limit of CI	*P*
Age	1.018	0.99	1.03	0.057
BMI	1.01	0.97	1.06	0.488
Clinical tumor size	0.99	0.98	1.007	0.374
eGFR	1.003	0.99	1.01	0.426
PADUA score				
12/13	Reference			
10	2.70	1.41	5.2	0.003
11	1.54	0.87	2.74	0.136
Tumor face				
Anterior	Reference			
Posterior	0.64	0.39	1.04	0.070
Access				
Transperitoneal	Reference			
Retroperitoneal	2.17	1.14	4.10	0.018

BMI=Body mass index, eGFR=Estimated glomerular filtration rate, CI=Confidence interval, OR=Odds ratio, PADUA=Preoperative aspects and dimensions used for an anatomical

function preservation. Longer WIT could lead to poor renal function preservation.[28] Nevertheless, a genuine attempt for PN seems reasonable because radical nephrectomy is the only plausible alternative for such renal masses. Intraoperative blood loss and the need for blood transfusion are within acceptable ranges and align with previous literature [Table 3].

Conversion to open surgery or radical nephrectomy was needed in 1 (0.2%) and 14 (2.7%) patients, respectively. A multicentric study of RAPN in complex renal masses by Buffi *et al*. had reported comparable rates of conversion to open (1.6%) and radical nephrectomy (1.9%).[17] In contrast, two single-center studies have reported higher rates of conversion to radical nephrectomy (5.2% and 5.7%).[15,21] Complication rates noted in the present research are similar to the literature for RAPN for complex masses [Table 3]. Furthermore, major complication rates noted in the present study are equivalent to those indicated in low-complexity tumor series.[15,29] We also noted that major complication rates were higher in patients with a high PADUA score of 12 and 13 (5.1% vs. 0.6% vs. 1.9%). On the contrary, Buffi *et al*.[17] and Koukourikis *et al*.[21] noted no change in overall complications with increasing PADUA score.

Positive surgical margin in the present study was seen in 10.3% of the patients. In addition, positive surgical margins were significantly higher in transperitoneal RAPN. However, there was no difference in positive surgical margins according to the PADUA scores [Table 2]. This rate is at a higher range of values of similar case series, as shown in Table 3. The reasons for these high positive surgical margin rates in the present study are unclear. It could be attributed to tumor complexity, surgeon experience, and surgical technique (excision or enucleation). However, data for the latter two factors are not available from the present study. Surgical margins have been considered proxy markers for adequacy of surgical resection. However, their impact on oncological outcomes remains debatable.[30]

Trifecta outcomes were achieved in 60.7% of the patients. As discussed previously, WIT was the most common cause of failure. Which suggests satisfactory excision of complex tumors and repair of remnant renal parenchyma is time-consuming. Patients with PADUA score 10 and 11 had higher trifecta compared to PADUA12/13. Similar to our study, Buffi *et al*.[17] noted significantly lower trifecta outcomes for PADUA scores of 12 and 13 compared to PADUA scores of 10 and 11. On the contrary, Koukourikis *et al*.[21] did not find any difference in trifecta outcomes according to PADUA scores in patients with complex renal masses. We also noted significant variability (37.5%–75.5%) in the rates of trifecta outcomes for various case series of RAPN in complex renal masses [Table 5]. This could be attributed to different definitions of trifecta outcomes used in multiple studies [Table 5]. Interestingly, in the present study, of the seven factors studied, we noted only surgical access (retroperitoneal or transperitoneal) and PADUA score to be an independent predictor of the trifecta. Trifecta outcomes noted in the present study compare well to previous RAPN literature.[16,17,31]

Limitations

Despite being one of the most extensive series in patients with complex renal masses undergoing RAPN, this study has limitations. Being a retrospective study, it is susceptible to selection bias. This may be the most plausible explanation for better perioperative outcomes with retroperitoneal than transperitoenal approach. Data to VCQI are contributed by different centers across the country. This may account for heterogeneity in surgical techniques, learning curves, perioperative management, and follow-up guidelines of the patients. The database lacks information on surgeon experience and center volume. Data are also lacking on the modality used for reporting tumor size and tumor complexity score. Furthermore, data on who calculated the RENAL nephrometery score are also not available. Due to the retrospective and multicentric nature of the study, a central review of all the radiology was impossible. There is a lack of data on operative details, such as the technique of resection enucleation versus resection versus enucleoresection. Details on clamping technique (selective, superselective, artery only, or *en masse* clamping) and model of robot (Si, X, or Xi) is lacking. Data precisely for hilar and completely endophytic tumors are also lacking from the database. The use of adjunctive techniques such as intraoperative ultrasound and frozen section is also lacking in database. Finally, the study also lacks functional and oncological data. In view of shortcoming in the VCQI database in its current format, further studies would be essential with upgraded database.

Table 5: Perioperative outcomes following robot-assisted partial nephrectomy in studies with high complexity renal masses (radius, endophytic/exophytic, nearness, anterior/posterior location or preoperative aspects and dimensions used for an anatomical score ≥10)

Study year (*n*)	Duration (min), mean	Blood loss (ml), mean	Blood transfusion (ml), *n* (%)	WIT (min), mean	Grade I or II complication, *n* (%)	Grade III, IV complication, *n* (%)	Hospital stay (days), mean	Margin positivity, *n* (%)	Trifecta (%)	Trifecta definition
Garisto *et al.*, 2018[18] (203)	208	200	6 (2.9)	28	43 (21.1)	14 (6.9)	3	18/179 (10)	-	-
Hennessey *et al.*, 2017[19] (31)	155	200	-	23	2 (6.4)	0	3.5	1 (3.2)	-	-
Kim *et al.*, 2019[20] (85)	150	200	8 (9.4)	24	8 (9.4)	10 (11.7)	5	0		
Raheem *et al.*, 2016[15] (121)	164	360	10 (8.2)	26	20 (16.5)	6 (4.9)	5.6	12 (9.9)	37.5	WIT of <25 min and negative surgical margins and absence of intraoperative and major postoperative complications
Schiavina *et al.*, 2017[7] (79)	169	243	-	24.7	2 (2.5)	4 (5)	-	-	-	-
Simhan *et al.*, 2012[22] (10)	221	225	-	33.8	-	-	3.7	0	-	-
Tomaszewski *et al.*, 2014[23] (24)	215	262	-	36.1	-	-	-	-	-	-
Ubrig 2018[32] (212)	193.7	-	3 (1.4)	15.5	35 (16.5)	19 (8.9)	-	13 (6.1)	75.5	WIT of<20 min and negative surgical margins and absence of major postoperative complications
Volpe *et al.*, 2014[25] (44)	132.5	381	2 (4.5)	18	6 (13.6)	4 (9)	7.7	2 (4.5)	-	-
White *et al.*, 2011[26] (11)	201	456.25	-	27	-	-	4	1 (9)	-	-
Beksac *et al.*, 2019[16] (144)	214.6	168.75	1 (0.69)	20.25	12 (8.3)	3 (2.3)	1	8 (5.5)	61.8	WIT <25 min, no perioperative complications, and negative surgical margins
Buffi *et al.*, 2020[17] (255)	162	162.5	-	18.5	62 (24.3)	13 (5.1)	4	4 (1.9)	62	Absence of Clavien-Dindo >2 complications, WIT <20 min, and absence of positive surgical margins
Koukourikis *et al.*[33] (*n*=155)	150 (112-186)	250 (100-500)		26 (23-32)	13 (14.8)	2 (1.2)	4 (3-6)	10.5	43.2	WIT of<25 min and negative surgical margins and major postoperative complications
Current study (*n*=514)	173 (45-546)	150 ml (50-3500 ml)	2.1	21 (0-55)	6.6	2.1	3 (1-19)	10.3	60.7	WIT <25 min, no perioperative complications, and negative surgical margins

WIT=Warm ischemia time

CONCLUSION

RAPN is an acceptable surgical option in patients with complex renal masses wherever feasible. It is associated with acceptable perioperative outcomes with an attendant risk of higher WIT and positive surgical margins.

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