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Conversion of robot assisted partial nephrectomy to radical nephrectomy; a prospective multi-
Institutional study

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Conflicts of Interest

Dr. Ronney Abaza reports grants from Conmed Inc., grants from Intuitive Surgical Inc., outside the submitted work; and Educational program support from Intuitive Surgical Inc.

Dr. Alexander Mottrie reports personal fees from Intuitive Surgery, outside the submitted work;

Dr. James R. Porter reports personal fees from Intuitive Surgery, outside the submitted work;

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Abstract

Objectives: To assess the incidence, and factors affecting conversion from robot-assisted partial nephrectomy (RAPN) to radical nephrectomy.

Methods: Between November 2014 and February 2017, 501 patients underwent attempted RAPN by 22 surgeons at 14 centers in nine countries within the Vattikuti Collaborative Quality Initiative database. Patients were permanently logged for RAPN prior to surgery and were analysed on an intention-to-treat basis. Multivariable logistic regression with backward stepwise selection of variables was done to assess the factors associated with conversion to radical nephrectomy.

Results: Overall conversion rate was 25/501 (4.99%). Patients converted to radical nephrectomy were older (median age [interquartile range] 66.0 [61.0-74.0] vs 59.0 [50.0-68.0], $P=0.012$), had higher body mass index (median 32.8 [24.9-40.9] vs. 27.8 [24.6-31.5] Kg/m^2 , $P = 0.031$), higher age-adjusted Charlson comorbidity score (median 6.0 [4.0-7.0] vs. 4.0 [3.0-5.0], $P < 0.001$), higher American Society of Anesthesiologists score (Score ≥ 3 ; 13/25 (52.0%) vs 130/476 (27.3%), $P = 0.021$), Preoperative estimated glomerular filtration rate ($P=0.141$), clinical tumor stage ($P=0.145$), tumor location ($P=0.140$), multifocality ($P=0.483$) and RENAL nephrometry score ($P=0.125$) were not significantly different between the groups. On multivariable analysis,

independent predictors for conversion were BMI (odds ratio [95% CI]; 1.070 [1.018-1.124]; $P = 0.007$), and Charlson score (odds ratio [95% CI]; 1.459 [1.179-1.806]; $P = 0.001$).

Conclusions: RAPN was associated with a low rate of conversion. Independent predictors of conversion were body mass index and Charlson score. Tumor factors such as clinical stage, location, multifocality, or RENAL score were not associated with increased risk of conversion.

Introduction

The gold standard treatment option for patients with a small renal mass is nephron sparing surgery (NSS), with robot-assisted partial nephrectomy (RAPN) increasingly being used for this indication.¹ Compared to laparoscopic partial nephrectomy, RAPN is associated with a lower blood loss, better estimated glomerular filtration rate (eGFR) preservation, and shorter hospital stay.²⁻⁴ The enhanced instrument articulation and three-dimensional visualization afforded by a robot have widened its use, especially in complex cases, larger tumors, solitary kidneys⁵ and also translates into a shorter learning curve.⁶⁻⁸

NSS is preferred over radical nephrectomy (RN) for small renal masses whenever possible because of equivalent oncological outcomes with a reduced risk of postoperative chronic kidney disease.⁹⁻¹¹ One inherent risk of NSS is the need to convert to RN. The rate of conversion to RN during RAPN has been quoted variably from 0% to 5.5%, which is lower than open partial nephrectomy (OPN) and laparoscopic partial nephrectomy.^{2,4,12} However, these studies have been limited to retrospective analyses, single surgeon, or single institutional design, and small sample sizes¹³⁻¹⁶. One recent study has quoted the conversion rate at 14.5%. However, this was based on administrative database with use of mannitol with radical nephrectomy as a surrogate marker for conversion¹⁷.

Identifying factors associated with conversion can potentially identify patients who are at a higher risk of conversion and help patient counseling and surgical planning. With this in mind, we evaluated the overall rate of intraoperative conversion of RAPN to RN in a large, multi-institutional prospective database. We also aimed to identify the preoperative and intraoperative patient and tumor characteristics associated with conversion to RN.

Material and methods

Data source and patient cohort

The Vattikuti Collective Quality Initiative is a collaboration of medical institutions from around the world collecting high quality prospective data on robotic surgery in a web-based database. Within this database, we prospectively identified 502 patients who underwent attempted RAPN by 22 surgeons from 14 centers across nine countries between November 2014 and February 2017. One case of conversion to open partial nephrectomy (OPN) was excluded, leaving 501 assessable patients. Ethical committee clearance for data collection was obtained at each participant center.

Definition of variables

The variables used in this study were preoperative parameters: namely, age (patient's age in years on the date of surgery), gender (male/female), side of surgery (left/right/bilateral), body mass index (BMI; kg/m^2), preoperative serum creatinine in mg/dL , age-adjusted Charlson Comorbidity Index, American Society of Anesthesiologists (ASA) score, clinical stage (defined according to the American Joint Committee for Cancer, 7th edition)¹⁸, tumor location (upper/mid/lower pole), multifocality (defined as two or more radiologically visible tumors in the same kidney preoperatively), RENAL score (radius, exophytic/endophytic properties,

nearness of tumor to the collecting system or sinus in millimeters, and anterior/posterior location relative to polar lines)¹⁹, and estimated glomerular filtration rate (eGFR) calculated using the Cockcroft-Gault formula.²⁰ Operative variables used were the surgical approach used (retroperitoneoscopic/transperitoneal), estimated blood loss in milliliters, warm ischemia time (defined as time from the clamping of the main renal artery until unclamping in minutes), and total operative time (time from incision until the placement of the last skin suture).

All patients were suitable candidates for RAPN for a confirmed renal mass on preoperative imaging using computerized tomography. Tumors were staged using computerized tomography images confirmed by a radiologist. RENAL nephrometry scores were calculated using measurements from computerized tomography imaging.¹⁹ The planned procedure was permanently logged as RAPN prior to the date of surgery regardless of whether intraoperative conversion to RN was performed. The conversion to RN was logged prospectively.

Statistical analysis

Frequencies and proportions were reported for categorical variables. Medians and interquartile ranges were reported for continuously coded variables. Chi-squared and Wilcoxon sign rank test were used to compare the statistical significance of differences in categorical and continuous variables, respectively. The analysis proceeded in two steps. First, the baseline and operative characteristics were compared between the non-converted (group 1) and converted (group 2) cohorts. Subsequently, a multivariable logistic regression with backward stepwise selection of variables was done to assess the factors associated with conversion to RN.

In backward elimination, Wald test for individual variables is done. Variable with the least significant effect not meeting the level for staying in the model is removed. The process is repeated until no other effect in the model meets the specified level for removal.²¹

All statistical tests were assessed with a significance level of $P \leq 0.05$ or CI not including zero using SPSS version 21 (IBM Corp, Armonk, NY).

Results

The rate of conversion from intended RAPN to RN was 4.99% (25 of 501 patients). Twenty four were performed robotically and one using open technique. In addition to these 25 conversions to RN, one case was converted to OPN due to a difficult tumor dissection and the presence of four renal arteries. This case was excluded from analysis, as noted above.

Table 1 describes patient and tumor characteristics of groups 1 and 2. Group 2 had a higher mean age at surgery (median [interquartile range]; 66.0 [61.0-74.0] vs 59.0 [50.0-68.0], $P = 0.012$), higher BMI (median 32.8 [24.9-40.9] vs. 27.8 [24.6-31.5] Kg/m^2 , $P = 0.031$), higher Charlson age-adjusted comorbidity score (median 6.0 [4.0-7.0] vs. 4.0 [3.0-5.0], $P < 0.001$), and was more likely to have an ASA score of three or greater (13/25 (52.0%) vs 130/476 (27.3%), $P = 0.021$). Sex ($P = 0.192$), and preoperative eGFR ($P = 0.141$) were not found to be statistically different between both groups. Tumor characteristics, which included clinical tumor stage ($P = 0.145$), tumor side ($P = 0.659$), tumor pole location ($P = 0.140$), multifocality ($P = 0.483$), and RENAL score ($P = 0.125$) were not statistically different between the groups.

Table 2 compares intraoperative characteristics between the 2 groups. Estimated blood loss was comparable in both groups (median 100 [50-200] vs. 100 [80-200] ml, $P = 0.964$). There was no association between conversion and choice of access ($P = 0.534$). Out of the 25 converted cases, only four were converted after the application of clamp. The warm ischemia times in these patients were 15, 20, 20, and 30 minutes. The operative time was significantly higher in the converted group ($p=0.011$).

On multivariable analysis with backward stepwise selection of variables, independent predictors for conversion were BMI (odds ratio [95% CI]; 1.070 [1.018-1.124]; $P = 0.007$), and Charlson score (odds ratio [95% CI]; 1.459 [1.179-1.806]; $P = 0.001$). Age, and ASA score were not significant independent predictors of conversion (Table 3).

Comment

The conversion rate of RAPN has been reported variably in various retrospective studies.^{2,4,12} However, studying RAPN conversion in a retrospective setting is subject to reporting bias, as some procedures may be logged as the final procedure performed rather than the intended procedure with conversion, effectively decreasing the reported conversion rate. On the other hand, in administrative databases, this rate might be artificially increased due to upcoding or surrogate definitions for conversion.¹⁷ Our study is unique in that it is based on a database where the intended procedure is permanently logged into a web-based system prior to surgery. To our knowledge, this is the first prospective, multi-institutional study evaluating the conversion of RAPN to RN.

Our study had several interesting findings. First, the rate of conversion of RAPN to RN was 25/501 (4.99%). This rate is higher than 1.5% reported in a systematic review and meta-analysis by Choi *et al.*, and consistent with other studies where reported rates ranged from 0% to 5.5%.^{2,4,12-16} The higher conversion rate can be explained by our methodology where patients were permanently logged for RAPN prior to surgery and analysed on an 'intention-to-treat' basis. Changes in surgical planning to RN either by surgeon discretion or patient request between initial consult and surgery would be represented in our conversion rate. Thus, our rate is a robust representation of conversion based on the urologist's initial plan for RAPN. Additionally, cases with a higher suspicion for requiring RN may still be boarded as a RAPN on the basis of offering

the possibility of NSS if the tumor is found to be amenable to resection, with a low threshold for conversion. Given the ~5% chance of conversion in our study, possibility of conversion may be included in the consent for all patients. Since these cases were documented as RAPNs converted to RN, this potentially includes some cases which would have otherwise been labeled RN, potentially inflating our rate. We believe this NSS-first approach to be common practice as there is no obvious disadvantage to treating cases as such prior to tumor visualization. In fact, Kara *et al.* observed that 71.9% of conversions were anticipated preoperatively, which indicates that many reported conversions may be a consequence of the expanding indications of NSS.¹² Moreover, since the standardization of NSS in renal masses < 4 cm in 2009 and its increasing emphasis under the 2017 American Urological Association guidelines, patients who could have undergone RN are now afforded RAPN even for complex tumors.^{1,22} Indeed, favorable outcomes have been reported in large > 4 cm, hilar, multifocal, and completely endophytic tumors, which has significantly broadened the feasibility of RAPN.²³⁻²⁵ Our study encompasses a sizeable portion of such difficult cases; 27.3% of the total caseload (137 cases) involved clinical tumor stage T1b or greater, 63.7% (319 cases) had at least a medium RENAL score, and 38 cases were multifocal. Growing surgeon comfort with carrying out a more difficult RAPN rather than defaulting to RN would contribute to a higher conversion rate, although the benefit of this approach in terms of overall survival is not clear.^{26,27} If it appears that the RAPN will be challenging, surgeons should consider the approach they feel the most comfortable to accomplish the goals for their patient (open/robotic or referral to experienced center) in either approach. Taken together, our findings suggest that conversion remains low, even for challenging tumors and these rates are comparable to existing literature.^{2,4,12-16} The conversion rate is significantly lower than Khandwala, et al, who used the definition of conversion as an event in which patients

were administered mannitol but received radical nephrectomy.¹⁷ This definition is prone to upcoding, as well as downcoding potentially altering “conversion” rate.

Another interesting finding in the present study was that estimated blood loss was not significantly different between the converted and non-converted patients. This might be due to the fact that the decision to convert is mostly taken after visualization of tumor, after which the hilum is controlled, directly proceeding to RN. Although the database is limited in descriptive details of complications, bleeding was listed as a reason for conversion in only two cases, and out of 25 converted cases, only 4 had clamp application before conversion, which supports that most conversions were not due to bleeding, and the decision to convert was likely made at an earlier stage prior to clamping. In addition, our results indicate that the operative time was higher in the converted group compared to the non-converted group. Considering the fact that in general, the time taken to do a radical nephrectomy is shorter than partial nephrectomy due to lesser steps of surgery, the finding that operative time in converted cases was, in fact, higher, reflects the possible failure to progress in these cases.

Patient age, BMI, Charlson score, and ASA score were significantly different between the groups. It is worth noting that median preoperative eGFR in the two groups was not significantly different, indicating that preoperative renal function does not associate with risk of conversion. This finding suggests that all eligible patients were afforded NSS and eliminates a possible selection bias noted by Galvin *et al.*, whereby patients with poor renal function were more likely to have NSS, and thus a higher risk for conversion, while those with good function were more likely to receive RN outright.¹⁴

Interestingly, our analysis failed to identify an association between conversion and tumor characteristics, such as preoperative RENAL scoring, tumor location, tumor side, and

multifocality. Similar findings have been observed by Png *et al.*, who reported no association between RENAL score and RAPN complication rates, blood loss, conversion rate, and postoperative decrease in eGFR.²⁸ In addition, Komminos *et al.* reported no association between RENAL score and prediction of major complications for complex, completely endophytic tumors.²⁴ Notably, of the 38 multifocal RAPNs in our study, only one (4.0%) resulted in conversion. Thus, a complex tumor does not necessarily indicate a higher risk of conversion and clinicians should continue to prioritize NSS approaches whenever possible. Current literature on the relationship between RENAL score and operative complications including conversion are equivocal. Our conclusions regarding tumor complexity and conversion differ from a similar retrospective, single-institution study of 1023 RAPNs from 2010 to 2015 conducted by Kara *et al.* that reported a conversion rate of 3.1% with an association with RENAL score.¹² One conversion was performed open due to intraoperative findings of a renal vein thrombus. Their finding is not surprising as complex tumors present a technical challenge to the surgeon and other studies have reported a similar association.^{7,14} By comparison, our study encompasses a more recent pool of RAPNs from 2014 to 2017. It is possible that recent refinements in surgical technique and greater experience in negotiating complex tumors has led to a relative equalization in conversion risks.

On the multivariable analysis, only BMI and Charlson score were found to be independently associated with conversion. Higher body mass index is usually associated with a larger amount of perinephric and hilar fat, which might possibly make delineation of the tumor more challenging. BMI may be a surrogate for other medical comorbidities. If a patient has multiple medical comorbidities and a tumor that would require a prolonged operative time and potential for complications that might not be well tolerated, a surgeon might have a lower threshold to

convert to radical nephrectomy, particularly if the renal function was normal. Our findings differ from previous studies which found no association between conversion and body mass index for minimally invasive partial nephrectomy.^{29,30} With a higher number of comorbidities, the incremental benefit of partial nephrectomy over radical nephrectomy with a normal functioning contralateral kidney is questionable.^{26,27} Many of these patients have limited life expectancy, and thus, possibly a low threshold for RN is maintained.

The findings of our study should be interpreted within the limitations of the observational study design. Our database contained incomplete information regarding the reasons for intraoperative conversion, details of intraoperative events leading to conversion, and whether or not the conversions were anticipated by the surgeon preoperatively. However, we believe that despite being a secondary analysis of a database which was not specifically built to answer the present research question, the study does add valuable insights into the true likelihood of conversion and potential predictive factors for conversion. Given the rarity of a conversion event, the conversion group was small. However, to avoid overfitting of the model, a stepwise backward elimination of variables was done. Despite these limitations, our study remains the only prospective, multi-institutional series to investigate RN and open conversion as well as predictive factors.

Conclusions

To summarize, RAPN conversion to RN is rare even in challenging tumors, with a rate of 4.99% using a prospective, multi-institutional, intention-to-treat analysis. Conversion was associated with BMI and Charlson age-adjusted score. Clinical tumor stage, location, multifocality, or RENAL score were not associated with increased risk of conversion.

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Table 1: Patient and tumor characteristics of converted and non-converted robot assisted partial nephrectomy in 501 patients operated at multiple centers in the Vattikuti Collective Quality Initiative database between November 2014 and February 2017.

Analysis	No Conversion	Conversion	P
	N=476	N=25	
Age at surgery, years, median (IQR)	59.0 (50.0-68.0))	66.0 (61.0-74.0)	0.012
Number of males, <i>n</i> (%)	327 (68.7)	14 (56.0)	0.192
Body mass index (n=496), kg/m ² , median (IQR)	27.8 (24.6-31.5)	32.8 (24.9-40.9)	0.031
eGFR, mL/min/1.73m ² , median (IQR)	77.3 (65.8-91.8)	71.4 (52.6-88.6)	0.141
Charlson age-adjusted score (n=322), median (IQR)	4.0 (3.0-5.0)	6.0 (4.0-7.0)	<0.001
ASA score, <i>n</i> (%)			0.021
1	104 (21.8)	2 (8.0)	
2	241 (50.6)	10 (40.0)	
3-4	130 (27.3)	13 (52.0)	

Clinical tumor stage, <i>n</i> (%)			0.145
T1a	350 (73.5)	14 (56.0)	
T1b	110 (23.1)	10 (40.0)	
≥T2b	16 (3.4)	1 (4.0)	
Side of tumor, <i>n</i> (%)			0.659
Left	228 (47.8)	12 (48.0)	
Right	233 (48.9)	13 (52.0)	
Bilateral	15 (3.2)	0 (0.0)	
Tumor location, <i>n</i> (%)			0.140
Upper pole	156 (32.8)	13 (52.0)	
Mid pole	164 (34.5)	6 (24.0)	
Lower pole	156 (32.8)	6 (24.0)	
Multifocality, <i>n</i> (%)			0.483
Unifocal	436 (91.6)	25 (96.0)	
Multifocal	37 (7.8)	1 (4.0)	
RENAL nephrometry score, <i>n</i> (%)			0.125

Low, 4-6	174 (36.5)	7 (28.0)	
Medium, 7-9	245 (51.5)	11 (44.0)	
High 10-12	56 (11.8)	7 (28.0)	

IQR: Interquartile range; eGFR, estimated glomerular filtration rate; ASA, American Society of Anesthesiologists; RENAL: radius, exophytic/endophytic properties, nearness of tumor to the collecting system or sinus in millimeters, and anterior/posterior location relative to polar lines.

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Table 2: Intraoperative characteristics of converted and non-converted robot assisted partial nephrectomy in 501 patients operated at multiple centers in the Vattikuti Collective Quality Initiative database between November 2014 and February 2017.

Analysis	No Conversion N=476	Conversion N=25	P
Access, <i>n</i> (%)			0.534
Transperitoneal	402 (84.5)	20 (80.0)	
Retroperitoneal	73 (15.3)	5 (20.0)	
Estimated blood loss, ml, median (IQR)	100 (80-200)	100 (50-200)	0.964
Operative time, minutes, median (IQR)	166 (140-200)	220 (158-255)	0.011

IQR, interquartile range

Table 3: Univariable and multivariable Logistic regression analysis predicting conversion to radical nephrectomy in 501 patients who underwent attempted robotic-assisted radical nephrectomy at multiple centers in the Vattikuti Collective Quality Initiative database between November 2014 and February 2017.

Analysis	Univariable analysis		Multivariable analysis	
	OR (95% CI)	P	OR (95% CI)	P
Age, years	1.046 (1.009-1.084)	0.013	Eliminated	-
Body mass index, kg/m ²	1.067 (1.018-1.119)	0.007	1.070 (1.018-1.124)	0.007
Charlson age-adjusted score	1.386 (1.147-1.675)	<0.001	1.459 (1.179-1.806)	0.001
ASA Score ≥3 (Ref = score 0-2)	2.335 (1.233-4.422)	0.009	Eliminated	-

CI: Confidence intervals; ASA, American Society of Anesthesiologists; OR, odds ratio