Int Urol Nephrol (2013) 45:381–385
DOI 10.1007/s11255-013-0392-4

UROLOGY - ORIGINAL PAPER

A comparison of pathologic outcomes of matched robotic and open partial nephrectomies

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Received: 20 December 2012 / Accepted: 22 January 2013 / Published online: 6 February 2013

Abstract
Purpose Open partial nephrectomy (OPN) and robotic partial nephrectomy (RPN) are widely utilized techniques for small renal masses. The lack of tactile feedback and limitations of laparoscopy may result in differences in the surgical specimen that may impact oncologic outcome. We present postoperative pathological outcomes data in a cohort of patients matched for nephrometry score, tumor size, gender and age.
Materials and methods We reviewed 81 patients who underwent partial nephrectomy between January 2003 and March 2010. Twenty-seven underwent RPN and 54 received OPN. Two OPN cases were matched for nephrometry score, tumor size, gender and age for each RPN. Postoperative pathological specimens were reviewed by a urologic pathologist regarding margin status, pathologic stage, histology, renal capsule violation, among other variables.
Results Sixty-two (76.5 %) patients were found to have renal cell carcinoma on final pathology. Frozen sectioning with tumor bed sampling was intra-operatively employed in 70 cases (86.4 %). The overall positive margin occurrence was 1 of 81 patients, which occurred during an RPN for a hilar tumor and converted to radical nephrectomy to achieve negative clinical margins. Additionally, 14.8 % of OPN patients had renal capsule violation as compared to 3.7 % of RPN cases ($p = 0.34$). Importantly, the mean distance to the proximal margin edge for RPN specimens (2.77 mm) was equivalent to OPN (3.01 mm), $p = 0.46$.
Conclusion When matched for nephrometry score, tumor size, gender and age, RPN produces similar pathological outcomes to OPN.

Keywords Margin · Partial nephrectomy · Pathology

Abbreviations

OPN	Open partial nephrectomy
RPN	Robotic partial nephrectomy
LPN	Laparoscopic partial nephrectomy
RCC	Renal cell carcinoma
BMI	Body mass index
AML	Angiomyolipoma

Introduction

Open partial nephrectomy (OPN) has become the standard of care for small cortical renal tumors [1, 2].

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Recent studies have demonstrated the oncologic outcomes of partial nephrectomy to be similar to radical nephrectomy, leading to increased application of nephron-sparing techniques [3–5]. Robot-assisted partial nephrectomy (RPN) has emerged as an alternative to open approaches. Although technically challenging, a number of recent studies have produced acceptable renal function and pathologic outcomes [6, 7]. The technical difficulty during the initial robotic experience and the lack of tactile feedback could affect the partial nephrectomy specimen and impact pathologic outcomes that are not readily apparent in a typical pathology report.

Direct comparisons between OPN and RPN can be difficult due to tumor variability, patient characteristics and surgeon preference. In this study, we compare a detailed pathologic evaluation of the specimens of these two techniques in a cohort of patients matched for nephrometry [8] scores and other factors.

Materials and methods

Study design

A retrospective review of patients with T_{1a} renal lesions treated with RPN or OPN between January 2003 and March 2010 at Indiana University Medical Center was performed after Institutional Review Board approval. Patients with previous renal cancer or surgery, solitary kidneys or clinical evidence of metastatic renal cancer were excluded. All consecutive cases of robotic partial nephrectomy performed by a single surgeon (CPS) were included. For each RPN, two OPN's were matched in terms of patient age (within 10 years), gender, race, tumor size (within 0.5 cm) and nephrometry score (within 2). The preoperative characteristics of these two groups were compared to ensure similarity.

Pathologic review

All frozen-section and final pathologic specimens were blinded and reviewed by a urologic pathologist. Assessment of margin status was based on final pathology review. Pathologic specimens were examined via standard formalin fixation and paraffin embedding. Sectioning was performed at 3–5 μm. An Olympus BX-40 microscope was used, and distances were measured using standard micrometer to the nearest 10th of mm. Perinephric fat coverage was determined to be present or not present. If present it was divided into <33 %, 33–67 % and >67 % by visual estimation. Tumor encapsulation was characterized as either present or not present. For tumors abutting the renal capsule, these sections were examined for incomplete renal capsule and evidence of surgical cautery. Proximal margin distance was the measurement of the closest margin, and distal margin distance was measurement of the farthest distance. A positive surgical margin was defined as tumor cells present at the inked margin. Tumor classification was based on the currently recognized entities in the 2004 World Health Organization System [9]. The tumors were designated as oncocytoma, angiomyolipoma, papillary RCC, chromophobe RCC, clear cell RCC and RCC unclassified. When applicable, renal cell carcinomas were graded based on the Fuhrman system for classification by nuclear grade [10]. Tumor size was determined by measuring the longest transverse diameter of the tumor. Tumors were evaluated for the presence of encapsulation, renal sinus fat involvement and perinephric fat invasion. Additionally, specimens were designated as grossly intact or fragmented and evaluated for procedurally related renal capsule violation.

Statistical analysis

Categorical data were compared using the chi-squared test or Fisher's exact test. The Mann–Whitney or Kruskal–Wallis test was employed to compare median data between groups. A p value < 0.05 was considered statistically significant.

Results

A total of 81 partial nephrectomies performed between January 2003 and March 2010 were reviewed: 27 RPN and 54 OPN. Patient demographics are displayed in Table 1. The matched cohorts were similar with regard to mean age, gender, BMI, nephrometry score as well as existing comorbidities. The mean preoperative renal mass size was equivalent in each group (2.4 vs. 2.4 cm), $p = 0.89$. No mortality was observed.

The pathological features of the study cohort are represented in Table 2. The measured tumor sizes

Table 1 Patient demographics

	RPN (27)	OPN (54)	*p*
Mean age (years)	57.6	56.8	0.56
Female patients	8	16	1.00
Mean BMI (kg/m^2)	32.0	30.8	0.36
Mean renal mass size (cm)	2.4	2.4	0.89
Mean nephrometry score	6.0	6.0	0.98
Mean preoperative GFR (ml/min/1.73 m^2)	70.8	78.7	0.09
History of diabetes	5	6	0.36
History of hypertension	17	27	0.27

between groups were not statistically different ($p = 0.49$). Furthermore, the histological grade of removed specimens, tumor encapsulation, renal capsule violation or presence of perinephric fat overlying the tumor did not differ between RPN and OPN groups. Tumor bed biopsy with frozen sectioning was employed more frequently during RPN cases (96.3 %) as compared to OPN (81.5 %), $p = 0.07$. Specifically, frozen sections were taken at the base of the resection bed and sent off separately from the tumor. At our institution, this frozen pathologic evaluation was completed after formal '. Malignancy was identified in 76.5 % of the cases overall. RCC was encountered more frequently in the open partial nephrectomy cohort ($p = 0.04$) compared to robotic cases, although the total number of RCCs and oncocytomas for OPNs was statistically equivalent to RPN ($p = 0.29$). The majority of tumors in our series were T_{1a} (70.4 %) and Fuhrman grade II (61.7 %).

The occurrence of positive surgical margins was low in our series (1.2 %). Tumor was identified on the cut tumor surface of one RPN specimen. Due to its hilar location, the case was converted to radical nephrectomy to achieve negative clinical margins. Final pathology revealed multifocal RCC. Four OPN cases had tumor at the specimen margin. Three cases required additional deep margin sectioning which returned negative on both frozen and final pathology. One case revealed AML with no additional sections taken. Highly complex lesions (nephrometry score ≥ 8) regardless of cohort were more likely to have tumor at the specimen margin, when compared to all other lesions (15.8 vs. 3.8 %, $p = 0.08$). Importantly, neither the least nor the greatest surgical margin depths were different between the RPN and OPN groups, $p = 0.46$ and 0.44, respectively.

Discussion

The validity of robotic surgery for the spectrum of renal surgical disease has been widely accepted. In this study, we retrospectively compared pathologic outcomes for patients who underwent either open or robotic partial nephrectomy. In particular, these cohorts were matched for tumor size, nephrometry score, patient age and gender. Our analysis demonstrated no statistical differences existed between RPN and OPN based on a number of pathological parameters. A comparison of these groups revealed similar distribution of lesion complexity as the mean nephrometry score for each was 6.0, $p = 0.98$. Tumor size was very similar as well, only varying by 0.2 cm, suggesting very similar groups of patients receiving each of the two treatment modalities. Importantly, robotic partial nephrectomy did not represent increased incidence of capsular violation or positive margin status. Although our data show a difference in RCC occurrence in resection of RCC in OPN specimens (83.3 %) versus RPN cases (63.0 %), when oncocytomas are added to the comparison this difference becomes statistically insignificant. Given the fact these two tumors cannot be distinguished radiographically during preoperative planning, this finding may be spurious.

Traditional requirements have dictated the removal of at least 1 mm margin of healthy tissue around a resected tumor during partial nephrectomy [11]. This can be challenging during nephron-sparing procedures and there has been concern that the loss of tactile feedback during robotic cases may lead to increased violation of surgical margins. Although the appropriate width for surgical margins is controversial, our series suggest the RPN and OPN are equivalent in this regard. A recent study by Hagemann and Lewis [12] comparing margin evaluation during partial nephrectomy found similar results. Further, these authors suggest that the laparoscopic robotic approach predisposes the surgeon toward performing tumor bed biopsies and frozen sectioning as compared to open procedures. Our series also identified a similar finding as 96 % of RPNs utilized tumor bed biopsies whereas they were employed in 81.5 % of open cases,

Table 2 Pathological data

	RPN (27)	OPN (54)	*p*
Histology			
RCC	17	45	0.04
Clear cell	10	35	
Papillary	6	5	
Chromophobe	0	2	
Unclassified	1	3	
Other	10	9	
AML	3	2	
Oncocytoma	6	5	
Other	1^{α}	2^{β}	
Pathological stage (AJCC 2010)			
T_{1a}	13	44	0.01
T_{1b}	3	0	
T_2	0	0	
T_{3a}	1	1	
Fuhrman grade			
I	1	3	0.91
II	16	34	0.10
III	0	8	
IV	0	0	
Encapsulated tumor	13	33	0.30
Perinephric fat present	26	51	0.72
<33 % coverage	8	4	
33–67 %	1	7	
>67 %	17	40	
Frozen section utilized	26	44	0.07
Positive surgical margin	1	0	0.15
Tumor size (cm)	2.49	2.30	0.49
Renal capsule violation	2	8	0.34
Proximal margin distance, mean (mm)	2.77 ± 3.02	3.01 ± 2.75	0.46
Distal margin distance, mean (mm)	8.07 ± 3.36	7.41 ± 3.35	0.44

$^{\alpha}$ Metanephric adenoma, $^{\beta}$ multilocular cyst

$p = 0.07$. The specimen is usually not immediately removed after excision during the robotic approach and is available for inspection only after the renal reconstruction is complete. That could account for the increased use for frozen-section examination. One conclusion from the low numbers of positive margins in either arm of the study is that frozen sectioning is likely overutilized in this study. Although part of the routine surgical approach of the senior author, in only one case did the addition of this technique lead to resection and eventual conversion to radical nephrectomy during RPN. This observation also correlates with a recent study from the Cleveland Clinic which investigated the utility of frozen section during robotic partial nephrectomy [13]. Their group observed a similar low percentage of positive margins in cohorts with and without the use of frozen sections, suggesting a restricted benefit from this technique. Based on our results, we would agree that routine use of frozen sectioning is of limited utility.

Although there have been numerous series comparing laparoscopic and open partial nephrectomy techniques based on operative parameters and functional outcomes, there is little direct comparison of robotic partial nephrectomy to open. In particular, our series is the first to investigate specific pathological outcomes in these groups in a matched cohort. The largest series to date comparing LPN to OPN by Gill et al. [14] involved 771 laparoscopic and 1,028 open resections. The mean clinical tumor size for LPN was 2.7 cm (8.8 % > 4 cm) versus 3.5 cm (31.4 % > 4 cm) for OPN, which were also noted to be more central and endophytic. Positive margins were reported in 2.85 % LPN versus 1.6 % OPN. Additionally, our series is unique in its matched pathological comparison, utilizing the nephrometry score as a measure of tumor configuration [8] in addition to tumor size, patient gender and age. A recent series of 100 RPN cases was characterized by nephrometry score [15]. This series included tumors greater than 4 cm, and noted 6 % to have a nephrometry score of 10, which was rated as a highly complex lesion (score 10–12), and 45.7 % to have moderate complexity (score 7–9). They report a positive margin rate of 5.7 %. Our series noted an association between a nephrometry score ≥ 8 and a higher rate of tumor at the specimen margin, though these had negative additional tumor bed sampling.

A limitation of this study is the inherent selection bias of a retrospective review. Our goal was to compare pathologic outcomes of RPN with OPN. We chose to include consecutive RPN patients and match them with equivalent open cases done during the same time period. Different experienced oncologic surgeons performed OPN than the surgeon performing the RPN cases. This could lead to different outcomes based on variations in surgical technique. However, if one were to compare these two techniques by controlling for the surgeon, selection bias may ensue.

Also, the robotic series was the initial experience of an experienced laparoscopic surgeon compared to a mature series of open cases. Another major limitation of this study is the size of the cohort. Although we did not statistically detect differences between the operative techniques, this study is not adequately powered to identify subtle differences.

Conclusions

Despite the concerns over loss of tactile sensation and it effect on surgical margin and tumor integrity, robotic partial nephrectomy produces similar pathologic outcomes to open approaches with regard to surgical margin depth and uniformity as well as capsular violation.

Conflict of interest The authors declare they have no conflict of interest.

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