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Comparison of Open and Minimally Invasive Partial Nephrectomy for Renal Tumors 4–7 Centimeters

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Abstract

Background: Indications for partial nephrectomy (PN) in the treatment of renal cell carcinoma are evolving, particularly for larger, more complex tumors.

Objective: Compare single-institution outcomes for minimally invasive partial nephrectomy (MIPN) and open partial nephrectomy (OPN) for tumors >4–7 cm.

Design, setting, and participants: A total of 2290 patients underwent PN from 2002 to 2010 at Memorial Sloan-Kettering Cancer Center; 280 had >4–7 cm renal cortical tumors. Of these 280 patients, 230 had pT1b, 48 had pT3a, and 2 had angiomyolipomas; 226 underwent OPN and 54 underwent MIPN (16 robot-assisted and 37 laparoscopic procedures). Perioperative management was uniform on the clinical pathway. Perioperative data, clinicopathologic variables, complications within 30 d, and oncologic outcomes were reviewed.

Measurements: Estimated glomerular filtration rate (eGFR) was calculated using the Chronic Kidney Disease Epidemiology Collaboration equation. Complications were reported from prospectively collected data based on a modified Clavien system. The Fisher exact and Mann-Whitney *U* tests were used for descriptive statistical analysis. Kaplan-Meier methods were used to estimate survival.

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Results and limitations: Median follow-up for OPN and MIPN was 29 and 13 mo, respectively. There were no statistically significant differences in age, gender, preoperative American Society of Anesthesiologists score, laterality, histologic subtype, tumor size, tumor stage, or margin status between procedures. Univariate analysis revealed significantly greater values in the OPN group for preoperative eGFR, renal artery clamp time, estimated blood loss, use of renal hypothermia, and length of stay. Differences in overall survival and recurrence-free survival were not statistically significant; however, short median follow-up times limit comparison. There was no significant difference in the number of complications grade 3 ($p = 0.1$) or urine leaks requiring intervention ($p = 0.7$). Limitations include the retrospective nature of the study and the possibility of selection bias.

Conclusions: OPN and MIPN procedures performed in patients with tumors >4–7 cm offer acceptable and comparable results in terms of operative, functional, and convalescence measures, regardless of approach.

Keywords

Renal cell carcinoma; Partial nephrectomy; Radical nephrectomy; Small renal masses; Minimally invasive surgery

1. Introduction

Partial nephrectomy (PN) is the standard of care for small renal masses and selected larger tumors that are technically amenable to nephron-sparing techniques. With experience, the boundaries of what is considered manageable by PN have expanded to include more complex and challenging cases involving multiple, central, and larger masses. From an oncologic perspective, PN has been found to be comparable with radical nephrectomy (RN) for appropriately selected patients with small (<4 cm) renal cancers [1–3]. The preservation of renal function associated with PN [4–6], combined with equivalent oncologic outcomes and recognition of the association between chronic kidney disease (CKD) and medical morbidity [7,8], has led the American Urological Association and European Association of Urology to declare PN as the procedure of choice when feasible [9,10]. In selected series, PN for larger tumors (>4 cm) has been suggested to provide similar oncologic outcomes and complications rates to RN either by the open [11–14] or the laparoscopic approach [15–17].

Alterations and developments in surgical technique are often intended to minimize perioperative morbidity while optimizing oncologic outcomes. Minimally invasive partial nephrectomy (MIPN), for example, is associated with reduced postoperative pain and hospital costs while maintaining comparable 5-yr oncologic outcomes compared with open partial nephrectomy (OPN) [18,19]. These techniques appear transferrable to larger and more complex cases; at Memorial Sloan-Kettering Cancer Center (MSKCC), the indications for PN were initially limited to lesions <4 cm but have expanded progressively to include any lesion that is technically feasible to remove, including nearly 80% of pT1b cases in 2009. The current study evaluates a contemporary cohort of patients who underwent PN either by minimally invasive (robot-assisted or laparoscopic nonrobotic) or OPN for renal tumors that were >4–7 cm and confined to the kidney without vascular invasion (including pT1b and pT3a by the 2002 American Joint Committee on Cancer definition) [20,21].

Surgical complications as well as oncologic and functional outcomes were assessed and compared between these approaches.

2. Materials and methods

After institutional review board approval was obtained, we identified 2290 PN procedures performed by 15 urologic oncology surgeons at MSKCC between January 2002 and February 2010. Renal tumors >4–7 cm were identified in 280 (12%) of these patients, and their medical records were retrospectively reviewed. Of the 280 patients, 230 had pT1b, 48 had pT3a, and 2 had angiomyolipomas. A total of 226 underwent OPN and 54 underwent MIPN (16 robot-assisted and 37 laparoscopic procedures). These cases comprised 57% and 46% of patients treated surgically for tumors >4–7 cm by the open or minimally invasive approach, respectively, during this period.

Patient demographics (gender, age), clinical characteristics (body mass index, American Society of Anesthesiologists [ASA] score, history of diabetes or hypertension), surgical characteristics (estimated blood loss, renal artery clamp time, transfusion rates, use of renal hypothermia, conversion of laparoscopic procedure to open surgery and from PN to RN), postsurgical complications (up to 30 d after surgery), pathologic characteristics, oncologic (recurrence rates and cancer-specific mortality), and renal function outcomes (estimated glomerular filtration rate [eGFR]) were compared for each technique. All perioperative management and follow-up was uniform using a common clinical pathway. Complication data were prospectively collected and retrospectively audited using the modified Clavien scale [22,23]. Urine leak was defined as a persistent drainage of urine for >7 d postoperatively or percutaneous drainage of an urinoma [22]. The eGFR was calculated with the Chronic Kidney Disease Epidemiology Collaboration equation [24]. Chronic kidney disease was diagnosed according to the National Kidney Foundation Dialysis Outcomes Quality Initiative Clinical Practice Guidelines [25].

2.1. Surgical technique

Standard laparoscopic, robot-assisted, and open PN procedures were performed. The laparoscopic approach included modified flank position and a three- to four-port method of transperitoneal nephrectomy. The robotic approach was completed via transperitoneal or retroperitoneal access using four to five ports (camera port, working arm ports [with a third arm if required for exposure], and assistant port). Open procedures included a variety of incisions between the 10th or 11th interspace, with most of them mini-flank incisions at the 11th rib [26,27]. Vascular control was obtained with a bulldog clamp except in selected patients who did not undergo renal artery occlusion. Cold ischemia, when utilized, was achieved with the described techniques of ice slush in the open procedures and by cold intravascular perfusion for minimally invasive procedures [28]. Reconstruction of collecting system defects was completed with interrupted sutures, and parenchymal hemostasis was achieved with absorbable hemostatic agents in bolster configuration and matrix injection [29].

2.2. Statistical analysis

The baseline characteristics of the OPN and MIPN groups were compared using the Fisher exact test for categorical variables and the Mann-Whitney *U* test for continuous variables. The Kaplan-Meier method was used to estimate survival probabilities, and a Cox proportional hazards regression model was used to adjust for preoperative eGFR. Disease recurrence was defined as any documented radiographic growing mass or pathologically proven failure in the operative site, regional lymph nodes, or distant metastasis. All statistics were performed using IBM SPSS Statistics v.19 (IBM Corp., Armonk, NY, USA).

3. Results

Median follow-up for OPN and MIPN was 29 and 13 mo, respectively ($p < 0.001$). Preoperative characteristics were comparable between types of procedure (Table 1), although patients in the MIPN group had statistically lower preoperative eGFR (OPN: 68 ml/min per 1.73 m²; MIPN: 61 ml/min per 1.73 m²; $p = 0.01$). Patients undergoing OPN under ischemia conditions had significantly longer renal artery clamp time (42 min vs 37 min; $p = 0.006$) and use of renal hypothermia (78% vs 7%; $p = <0.001$) compared with MIPN (Table 2). Those undergoing MIPN required longer median operative times (OPN: 159 min; MIPN: 242 min; $p < 0.01$), although median postoperative length of stay was shorter (OPN: 4 d; MIPN: 3 d; $p = 0.007$).

There was a statistically significant difference in median estimated blood loss in the OPN group (400 vs 300; $p = 0.03$). Notably, nine of the patients requiring transfusions in the OPN group did not undergo renal artery clamping. Of the remaining 22 OPN cases receiving blood, 3 were transfused intraoperatively and 19 postoperatively for low hemoglobin levels or symptoms. Three MIPN patients required blood transfusions. Two were intraoperative for bleeding and ultimately were converted to an RN after open exploration was unsuccessful in controlling hemostasis.

Renal function at 6 mo after surgery (Table 2) was not significantly different between the techniques. Median eGFR change from baseline at 6 mo postoperatively was -10 ml/min per 1.73 m² and -5 ml/min per 1.73 m² for the OPN and MIPN group, respectively ($p = 0.5$). Most of the patients had pT1b renal cell carcinomas (Table 3). Postoperative pain medication data (Table 4) revealed no significant difference in the use of narcotics ($p = 0.4$) or acetaminophen ($p = 0.3$) when comparing OPN and MIPN patients. However, OPN patients used more ibuprofen equivalents ($p = 0.002$). Three MIPNs were converted to open (6%) with two of these resulting in RN. A total of four conversions to RN (7%) occurred in the MIPN group (two open as just cited and two laparoscopic); 27 planned OPN cases (12%) were converted to RN. No renal units were subsequently lost or removed.

There were no cancer-specific deaths. Two local recurrences and five metastasis events occurred in the OPN group (median: 2 mo to event) (Fig. 1). Only one metastatic event was noted in the MIPN group. On univariate analysis, we did not find any evidence that procedure type was associated with recurrence-free survival (RFS) (log rank 0.7).

There was no statistically significant difference in the number of complications grade 3 (OPN 7%; MIPN 15%; $p = 0.1$) or occurrences of urine leak requiring intervention (OPN 4%; MIPN 4%; $p = 0.7$) (Table 5). In the MIPN group, there were more overall complications across all grades (33% vs 20%; $p = 0.05$). The positive margin rate was not significantly different between techniques (OPN: 5%; MIPN: 4%; $p = 0.5$).

4. Discussion

Progress in surgical technique and an enhanced understanding the biology of renal masses has led to an increasing use of nephron-sparing surgical approaches [30] and minimally invasive techniques for larger [15,17] and more complicated renal masses [31]. The results of the present study suggests that MIPN and OPN surgical approaches for renal masses >4–7 cm are comparable, without a significant impact on critical outcomes including overall and cancer-specific survival (CSS), positive margin rates, rates of grade 3 complications, or rates of urine leak requiring intervention.

Our institutional management strategies for renal masses focus on approaches intended to account for tumor biology while optimizing functional renal preservation and local tumor control. Under these strategies, PN is currently considered and potentially executed for any renal mass whenever technically feasible, regardless of size. This is particularly true if the mass is exophytic or polar in location. The development of this experience, demonstrated graphically in Figure 2, has grown gradually, from <26% of cases in 2002 to 81% of both open and minimally invasive procedures by the end of 2009. Although technically more challenging in this setting, the data regarding outcomes presented here are similar to those previously reported for smaller renal masses treated surgically [21,22]. These outcomes likely represent the evolution of multiple learning curves related to patient management, including a more thorough preoperative assessment and hence more educated case selection, technical advances related to surgical technique and instrumentation, and cognitive growth related to an improved understanding of cancer biology and patient physiology. In combination, this gained experience appears to span both open and minimally invasive approaches, demonstrating that PN for larger tumors is feasible with results that may be independent of surgical approach.

The primary limitation of our study is its retrospective nature, with the inherent limitations of a single-center nonprospective nonrandomized series. It is particularly difficult to account for biases including case selection, case complexity, and surgical learning curve. The concept of controlling for case complexity with nephrometry scoring systems [32] is of interest, yet these systems await validation and are of limited use in homogeneous cohorts like ours: The patients evaluated in this study all had tumors >4–7 cm that were deemed amenable to PN.

There are inherent difficulties with any comparative study of open and minimally invasive techniques. The open surgical experience is certainly more mature, which makes a controlled comparison with the earliest experience with both laparoscopic and robotic procedures inherently difficult. However, the similar growth curves in adapting to PN procedures for these larger tumors from 4 to 7 cm is indicative of a broader institutional

evolution in approach to renal masses. Despite these limitations, we see little in the way of differences in outcomes between the two approaches at our center. There has not been a shift in case volume away from open procedures over time, but instead there has been a parallel growth in minimally invasive procedures. A prospective multi-institutional randomized trial would be the best way to evaluate if surgical approach affects short- and long-term outcomes.

Oncologic outcomes are of primary concern in the surgical approach to renal tumors, both large and small. There were no cancer-related deaths in these patients, but our RFS rates were 94% in the MIPN group and 96% in the OPN group at 5-yr follow-up, which are consistent with rates seen in other series evaluating individual surgical techniques. Leibovich et al [14] reported a 5-yr CSS rate of 95% and 98% for patients with tumors measuring 4–7 cm who had undergone open PN and open RN, respectively. In a series comparing laparoscopic RNs and PNs for tumors ≤ 4 cm, Simmons et al [17] described a 97% CSS rate in both groups at a median follow-up of 57 mo and 44 mo, respectively. Becker et al [33] found overall survival to be 95% and CSS 100% at 5 yr for patients receiving OPN.

Positive margin rates for both the OPN and MIPN groups were 5% and 4%, respectively. In other published series, positive margin rates range from 1.3% [2] to 3.8% [34] for patients who underwent OPN for pT1b tumors, whereas positive margins for pT1b lesions in laparoscopic series range from 0% to 5.3% [15–17]. The published robotic series for lesions >4 cm had no positive margins [35,36], which may to a certain extent reflect case selection (our robotic series also had no positive margins). In the final years of this series, we treated approximately 80% of tumors >4 –7 cm with PN, indicating an ambitious nephron-sparing surgical program that includes deep tumors found within the renal hilum and central sinus, and may in part explain the slightly higher positive margin rates in this series.

A significantly longer renal artery clamp time was noted in the OPN compared with the MIPN group (42 min vs 37 min; $p = 0.006$) which differs from some of the published literature [37], although it is consistent with other series [18]. We believe a large contributing factor was the significant use of renal hypothermia (78% vs 7%; $p = <0.001$) in the OPN group compared with MIPN (Table 2). In the Cleveland Clinic experience [37], almost all PNs are done under warm ischemia, in which a shorter ischemia time has clearly been linked to improved renal functional outcomes [38]. In addition, the preoperative difference in eGFR between our two study groups was statistically significant, although the median 6-mo postoperative eGFR was within the range for stage 3 CKD in both groups. The degree of decrease related to surgery was similar to that in the published literature [39].

PN can be performed safely although with some increased risk of unique complications [22] compared with RN. Published data from patients with tumors ≤ 4 cm identify a 12% rate of surgical complications and a 5% rate of urinary fistula [2] for OPN; complication rates for laparoscopic series appear to range from 20% to 37% [16,17] with a urinary fistula rate of 7% [16]. This appears comparable with the one study of robot-assisted PN for tumors ≤ 4 cm that cites a urinary fistula rate of 5% [35]. Our standardized prospective institutional complication reporting system with use of detailed retrospective review criteria for adverse events previously demonstrated a higher rate of actual adverse event detection and reporting

[40]. This may account for the higher observed rate of overall complications relative to other published reports, although less so our rate of grade 3 complications (OPN 7%, MIPN 15%) that compares with events in other large series [2]. The association between complications and medical comorbidities is well documented, and the proportion of higher ASA scores in this series are notable, with scores >3 in 44% and 56% of OPN and MIPN cases, respectively, compared with 35% of those reported in other combined series [2].

5. Conclusions

With appropriate experience, PN for renal tumors >4–7 cm can be safely utilized in most cases by either open or minimally invasive surgery with comparable oncologic and functional outcomes regardless of choice of approach.

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Take-home message

Open and minimally invasive partial nephrectomy (PN) for tumors 4–7 cm in size appear to be comparable in terms of operative, functional, and convalescence outcomes. PN for larger renal lesions is an appropriate alternative to radical nephrectomy for many cases when performed by experienced surgeons, regardless of surgical approach.

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Time	0	2	4	6	8
Number at Risk					
OPN	226	133	66	27	2
MIPN	54	14	5	0	0

Fig. 1 –. Recurrence-free survival comparing open partial nephrectomy versus minimally invasive partial nephrectomy.

MIPN = minimally invasive partial nephrectomy; OPN = open partial nephrectomy.

Fig. 2 –. Change in utilization of partial nephrectomy as a percentage of all surgery (radical and partial nephrectomy) for renal masses pathologically >4–7 cm in size (pT1b and pT3a), 2002–2009.

MIS = minimally invasive surgery.

Table 1 –

Demographic and clinical characteristics of patients treated with partial nephrectomy for 4–7 cm renal cortical tumors

	OPN <i>n</i> = 226	%	MIPN <i>n</i> = 54	%	<i>P</i>
Age, yr					
Median (IQR)	61 (51–68)	-	59(51–67)	-	0.7
Gender					
Male	170	75	35	65	0.1
ASA score					
1 and 2	127	56	24	44	0.1
3 and 4	99	44	30	56	
BMI, kg/m ² , median (IQR)	29 (26–33)		31 (27–36)		0.06
Hypertension	118	52	27	50	0.8
Diabetes	30	13	9	17	0.5
Preoperative eGFR, ml/min per 1.73 m ² , median (IQR)	68 (55–78)	-	61 (53–68)	-	0.01
Laterality (left)	123	54	25	46	0.3
Length of follow-up, mo, median (IQR)	29 (14–53)	-	13 (6–25)	-	-

OPN = open partial nephrectomy; MIPN = minimally invasive partial nephrectomy; IQR = interquartile range; ASA = American Society of Anesthesiologists; BMI = body mass index; eGFR = estimated glomerular filtration rate.

Table 2 –

Perioperative characteristics of partial nephrectomies for 4–7 cm renal cortical tumors

	OPN		MIPN		P
	<i>n</i> = 226	%	<i>n</i> = 54	%	
Median estimated blood loss, ml, median (IQR)	400 (200–600)	-	300 (144–438)	-	0.03
Transfusion	33	15	3	6	0.1
Renal artery clamped	184	81	50	93	0.06
Renal artery clamp time, min, median (IQR)	42 (35–50)	-	37 (31–41)	-	0.006
Hypothermic ischemia	177	78	4	7	<0.001
Conversion					
To open	-	-	3	6	
To radical	27	12	4	7	0.5
Length of stay, d, median (IQR)	4 (3–5)	-	3 (2–5)	-	0.007
6-mo eGFR, ml/min per 1.73 m ² , median (IQR)	55 (43–65)		56 (51–74)		0.1
6-mo eGFR change in baseline, ml/min per 1.73 m ² , median (IQR)	-10 (-18 to -0.8)	-	-5 (-13 to +4)	-	0.5

OPN = open partial nephrectomy, MIPN = minimally invasive partial nephrectomy, IQR = interquartile range, eGFR = estimated glomerular filtration rate.

Table 3 –

Pathologic characteristics of patients who received a partial nephrectomy for 4–7 cm renal cortical tumors

	OPN		MIPN		<i>P</i>
	<i>n</i> = 226	%	<i>n</i> = 54	%	
Histology					
Clear cell	125	55	34	63	0.5
Papillary	39	17	7	13	-
Chromophobe	31	14	8	14	-
Unclassified	8	4	1	2	-
AML	2	1	0	-	-
Oncocytoma	18	8	1	2	-
Other	3	1	3	6	-
Tumor size, cm, median (IQR)	5.0 (4.5–5.5)	-	5.2 (4.5–5.9)	-	0.4
Positive margin	11	5	2	4	0.5
Stage					
pT1b	183	-	47	-	0.4
pT3a	41	-	7	-	-

OPN = open partial nephrectomy; MIPN = minimally invasive partial nephrectomy; AML = angiomyolipoma; IQR = interquartile range.

Table 4 –

Postoperative pain medication use of patients who received a partial nephrectomy for a T1b renal cortical tumor

	OPN	MIPN	<i>P</i>
Morphine equivalent, mg, mean $\pm$ SD	379 $\pm$ 637	343 $\pm$ 327	0.4
Acetaminophen equivalent, mg, mean $\pm$ SD	1297 $\pm$ 1056	2200 $\pm$ 2111	0.3
Ibuprofen equivalent, mg, mean $\pm$ SD	1972 $\pm$ 1103	927 $\pm$ 711	0.002

OPN = open partial nephrectomy; MIPN = minimally invasive partial nephrectomy; SD = standard deviation.

Table 5 –

Postoperative complication differences

	OPN (%)	MIPN (%)	OR	95% CI	<i>P</i>
Any complication	46 (20)	18 (33)	2.0	1.0–3.8	0.05
Grade 3 complications	16 (7)	8 (15)	2.3	0.9–5.7	0.1
Any urine leak	25 (11)	5 (9)	0.8	0.3–2.3	0.8
Urine leak requiring intervention	10 (4)	2 (4)	0.4	0.1–3.3	0.7

OPN = open partial nephrectomy; MIPN = minimally invasive partial nephrectomy; OR = odds ratio; CI = confidence interval.