

Laparoscopic Partial Nephrectomy for Renal Tumors Larger Than 4cm

Nefrectomia parcial laparoscópica para tumores renais maiores que 4 cm

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ABSTRACT

Background: Minimally invasive laparoscopic partial nephrectomy (LPN) is commonly performed for renal tumors d" 4 cm in size. LPN for tumors > 4 cm has not been assessed. **Objective:** To evaluate the safety and feasibility of LPN for tumors > 4 cm by comparing them to a group of patients undergoing LPN for tumors d" 4 cm. **Materials and Methods:** We reviewed data for 171 consecutive patients who underwent transperitoneal LPN between May 2002 and May 2012 performed by a single surgeon. Patients were stratified into two groups: 32 with tumors > 4 cm on preoperative imaging (group 1) and 139 patients with tumors d" 4 cm (group 2). Preoperative, perioperative, pathologic, and functional outcomes data were analyzed and compared between groups. We used X² and student t tests for categorical and continuous variables, respectively. A p value <0.05 was considered statistically significant. **Results:** Mean radiographic tumor size was 5.9 cm (4.1 – 9.2) for group 1 and 2.3 cm (0.9 – 4.0) for group 2. No significant differences were found between groups for estimated blood loss, total operative time, length of hospital stay, complication rates, and change in estimated glomerular filtration rate. Patients with larger tumors had longer median warm ischemia times (22 vs 17 min; p= 0.011). **Conclusions:** In our experience, LPN for tumors > 4 cm is safe and feasible, showing comparable outcomes to LPN for smaller tumors. More studies are necessary to determine the viability of LPN for large tumors as an effective form of treatment.

Key words: Laparoscopy. Nephrectomy. Partial nephrectomy. Renal cell carcinoma.

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1. INTRODUCTION

Nephron-sparing surgery has become an established approach for small renal tumors, demonstrating oncologic efficacy equivalent to that of radical nephrectomy (RN)¹⁻³ with the advantage of preservation of renal function and possibly improved survival. Laparoscopic partial nephrectomy (LPN) has demonstrated comparable oncologic and functional outcomes to open partial nephrectomy (OPN)⁴; however, partial nephrectomy (PN) for larger tumors may pose additional technical challenges during surgery. OPN has been described for patients with

tumors > 4 cm in size with satisfactory results.³ LPN has also been described for patients with tumors > 4 cm,^{5,6} but technical challenges may be even more pronounced with a laparoscopic approach than with an open approach. We evaluate early surgical, functional, and oncologic outcomes of LPN for renal tumors > 4 cm on preoperative imaging and compare these results to outcomes for tumors d" 4 cm.

2. PATIENTS AND METHODS

Data for 171 consecutive patients who underwent transperitoneal LPN at our institution

between May 2002 and May 2012 by a single surgeon (MBM) were reviewed from a prospectively maintained, institutional review board-approved database. Tumor size was assessed preoperatively with either computed tomography or magnetic resonance imaging. Patients were stratified into two groups based on clinical tumor size: 32 with tumors > 4 cm on preoperative imaging (group 1) and 139 patients with tumors $\leq$ 4 cm (group 2).

Pre-operative demographic factors analyzed included age, gender, surgical side, body mass index, history of previous abdominal surgery and American Society of Anesthesiologists classification. The tumor's location, endophytic nature, and proximity to the collecting system were assessed using preoperative imaging. The number of procedures performed for incidentally discovered masses and imperative indications (solitary kidney, bilateral renal masses, stage 3 or worse chronic kidney disease) was also assessed.

Our LPN technique reproduces the open procedure step-by-step. Briefly, patients are placed in flank position, and ports are placed as demonstrated in figure 1 for the right side and figure 2 for the left side.

Bowel mobilization and kidney exposure are performed. The renal hilum is dissected – and the perinephric fat is reflected to expose the kidney capsule – and then stretched for dissection of the renal vessels. Finally the kidney positioned for optimal tumor resection. The renal capsule is scored to demarcate the margins of the resection. Hilar occlusion is performed in all cases using either a laparoscopic bulldog clamp (Storz®) or a laparoscopic Satinsky clamp (Taimin®).

For large, endophytic, or central tumors, we generally clamp both the artery and the vein. For small, peripheral, cortical tumors, we sometimes clamp only the artery; when possible we clamp the terminal artery. Tumor excision is performed sharply with laparoscopic scissors, ensuring adequate surgical margins. In our series, the renal capsule was reapproximated using 0 polyglactin sutures anchored with Hem-o-lok clips (Teleflex Medical, Research Triangle Park, NC, USA) using the sliding clip renorrhaphy technique. The opposite side is secured by a Hem-o-lok clip to reapproximate capsular edges under tension. For larger tumors in which the excision leaves a wide defect, bolsters may be used.

Perioperative factors analyzed included total operative time (including abdominal insufflation, port

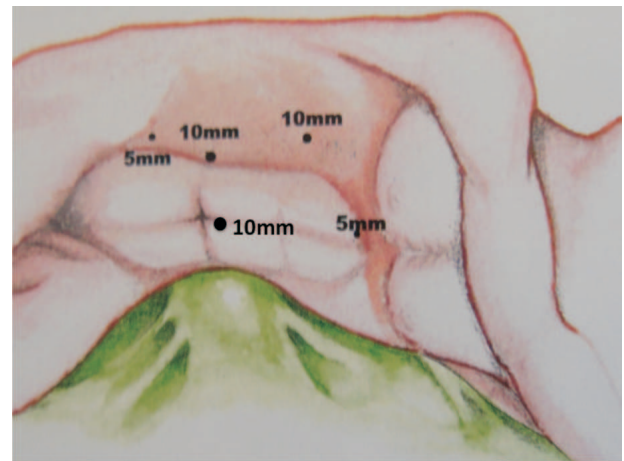


Figure 1 - Port placement during laparoscopic partial nephrectomy on the right side.

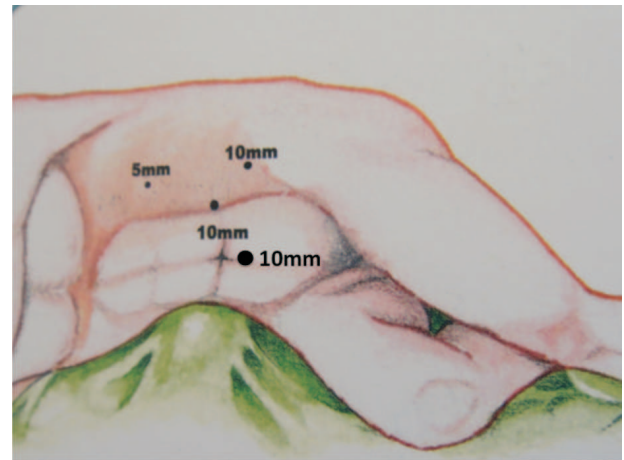


Figure 2 - Port placement during laparoscopic partial nephrectomy on the left side.

placement, specimen extraction, and closure), warm ischemia time, hilar clamping technique, estimated blood loss (EBL), conversion rate, change in hemoglobin 24 hours after surgery, length of hospital stay, and length of follow-up. Complications were recorded using the Clavien classification system.⁷ Change in the estimated glomerular filtration rate (GFR) from baseline was assessed 24 hours postoperatively and at follow-up visits one to three months after surgery using the Modification of Diet in Renal Disease formula.⁸ Pathologic factors analyzed included tumor size, histology, pathologic stage using the 2002 American Joint Committee on Cancer (AJCC) staging criteria, Fuhrman grade, and positive surgical margin rate.

Preoperative parameters and postoperative results as well as pathologic and functional outcomes data were retrospectively analyzed and compared

between groups. Statistical analysis was performed using Stata v.10 (StataCorp, College Station, TX, USA). Comparisons between groups were performed using X^2 and student t tests for categorical and continuous variables, respectively. A p value <0.05 was considered statistically significant.

3. RESULTS

A total of 171 patients underwent transperitoneal LPN at our institution during the study period, of which 32 patients had tumors larger than 4 cm on preoperative imaging. Baseline demographics and radiographic tumor characteristics are summarized in table 1. There was no significant difference in baseline characteristics between groups. Mean radiographic size was 5.9 cm (range: 4.1 – 9.2) and

2.3 cm (range: 0.9 – 4.0) for groups 1 and 2, respectively ($p < 0.001$).

Perioperative variables are summarized in table 2. Intraoperative variables, including EBL, clamping technique, and conversion rate, were similar between groups. One patient in group 2 with normal renal function and a normal contralateral kidney was converted from LPN to open nephrectomy because of difficulty encountered controlling the hilum with the laparoscopic clamp. All cases in both groups were performed under warm ischemia. The median warm ischemia time was longer for tumors > 4 cm (22 min vs 17 min; $p = 0.011$). The median total operative time was also longer for tumors > 4 cm (215 min vs 192 min) but did not attain statistical significance ($p = 0.068$). No patient required an intraoperative blood transfusion. Postoperative factors were similar

Table 1 – Preoperative variables for patients undergoing laparoscopic partial nephrectomy.

Characteristic		Group 1 (>4 cm)	Group 2 (≤ 4 cm)	p value
Patients , No.		32	139	-
Mean age in years (range)		58 (43-77)	62 (36-84)	0.675
Gender No. (%)	Male	20 (62.5)	83 (56.6)	0.868
	Female	12 (37.5)	56 (43.4)	-
Tumor side No. (%)	Left	21 (65.6)	92 (66.2)	0.663
	Right	11 (34.4)	47 (33.8)	-
Mean BMI, Kg/m ² (range)		31.6(19.5-48)	30.2(20.5-47)	0.726
ASA Classification score No. %	1	0 (0)	3 (2.2)	0.856
	2	13 (40.6)	52 (37.4)	
	3	19 (59.4)	84 (60.4)	
Previous abdominal surgery No. (%)	yes	5 (15.6)	36 (25.9)	0.278
	no	27 (84.4)	103 (74.1)	
Incidental finding No. (%)	yes	23 (71.9)	101 (72.6)	0.997
	no	9 (21.1)	38 (27.4)	
Imperative indication for PN No. (%)	yes	2 (6.3)	18 (12.9)	0.526
	no	30 (93.7)	121 (87.1)	
Radiographic variables				
Mean tumor size, cm (range)		5.9(4.1-9.2)	2.3(0.9-4.0)	<0.001
Tumor location within the kidney No. (%)	Upper	15 (47)	47 (33.8)	0.428
	Mid	8 (25)	59 (42.5)	
	Lower	9 (28)	33 (23.7)	
Percent endophytic No. (%)	$<50\%$	27 (84)	74 (53.2)	0.115
	$50 < 100\%$	5 (16)	50 (36)	
	100%	0 (0)	15 (10.8)	
Abutting collecting system, No. (%)	yes	23 (71.8)	79 (56.8)	0.275
	no	9 (28.2)	60 (43.2)	

Table 2 – Perioperative variables for patients undergoing Laparoscopic Partial Nephrectomy.

Characteristic	Group 1 (> 4 cm)		Group 2 (≤ 4cm)		p value	
Intraoperative variables						
Median total operative time, min (IQR)	215	(172-249)	192	(158-245)	0.068	
Median warm ischemia time, min (IQR)	22	(18-32)	17	(8-24)	0.011	
Median EBL, ml (IQR)	110	(80-215)	90	(40-210)	0.285	
Elective conversion No. (%)	1	(3)	0	(0)		
Clamping technique No. (%)	none	0	(0)	5	(3.6)	0.400
	Bulldog	4	(12.5)	7	(5.1)	
	Satinsky	28	(87.5)	127	(91.3)	
Collecting system repair No. (%)	yes	2	(6.2)	8	(6)	0.275
	no	30	(93.8)	131	(94)	
Postoperative variables						
Median length of stay, d (IQR)	2	(2-4)	2	(2-3)	0.196	
Mean change in hemoglobin 24 hours after surgery, g/dl(range)	-2.4 (-4.5 to 0.9)		-1.7 (4.0 to 0,7)		0.259	
duration of follow-up in months No. (range)	16	(0.9-45)	15	(0.3-45)	0.283	

IQR=interquartile range; EBL = estimated blood loss

between groups with regard to hospital stay, change in hemoglobin 24 hours after surgery, and follow-up. The overall mean follow-up for our study was 30 months; the longest duration of follow-up incorporated in the analysis was 120 months. There has been no renal-related mortality in our series to date (Table 3).

4. DISCUSSION

Partial Nephrectomy has demonstrated equivalent cancer control to Radical Nephrectomy for small renal masses,^{1,2} with improved long-term clinical, functional, and survival outcomes over RN.⁹⁻¹³ LPN, which was introduced in 1993,^{14,15} has emerged as a viable alternative for the surgical management of small renal masses, with oncologic and functional outcomes similar to OPN.^{4,16} However, LPN is technically challenging, requiring advanced skills to perform precise tumor excision and intracorporeal sutured reconstruction while minimizing ischemia times. Large tumors may present additional challenges during PN that may add to the challenges of LPN, including tumor resection and renal reconstruction under warm ischemia. A number of studies have demonstrated the feasibility of LPN.^{4,5,6,8}

Open PN for tumors > 4 cm has been reported with satisfactory results³, and initial reports in 2008 and 2009 from experienced surgeons demonstrated

the feasibility of the laparoscopic approach for these larger tumors.^{5,6} Our study is the first to evaluate LPN with a specific focus on patients with tumors > 4 cm and to compare outcomes with LPN for tumors < 4 cm.

Rais-Bahrami and cols.⁵ compared results of LPN for 34 patients with tumors > 4 cm and 274 patients with tumors ≤ 4 cm. There were no differences in preoperative characteristics or intraoperative outcomes between the two groups. Patients with larger tumors had more complications (32.3% vs 25.1%, $p=0.039$) and longer hospital stays (4.1 days vs 3 days; $p=0.026$). Simmons and cols.⁶ compared results of LPN for 58 patients with tumors > 4 cm to 278 patients with 2-4 cm tumors, and 89 patients with tumors < 2 cm. There were no statistically significant differences among the three groups in operative time, EBL, and length of hospital stay. Patients with larger tumors were more likely to require pelvicalyceal repair and had a longer mean warm ischemia times (38 min vs 30 min; $p=0.002$), but there was no differences in complications among the three groups.

In our study, patients undergoing LPN for renal masses > 4 cm had similar demographic and preoperative characteristics to patients undergoing LPN for smaller renal masses. Both groups had similar intraoperative outcomes. There was a

Table 3 - Comparison of intraoperative and postoperative complications.

	Group 1 (> 4 cm)		Group 2 (≤ 4 cm)		p value
Intraoperative complication No. (%)					
No	30	(94)	136	(97.9)	0.602
Yes	2	(6)	3	(2.1)	
Postoperative complication, No. (%)					
No	23	(71.9)	126	(90.6)	0.066
Yes	9	(28.1)	13	(9.4)	
Complication					
Intraoperative, No. (%)					
*Enterotomy No. (%)	0	(0)	2	(1.4)	
Postoperative, No. (%)					
Atelectasis No. (%)	0	(0)	2	(1.4)	
Urinary retention No. (%)	0	(0)	2	(1.4)	
**Urine leak No. (%)	4	(12.5)	0	(0)	
***Bleeding No. (%)	4	(12.5)	5	(3.5)	
Pulmonary embolism No. (%)	0	(0)	2	(1.4)	
Postoperative complication (Clavien classification) No. (%)					0.622
1	0	(0)	5	(3.5)	
2	2	(5.1)	2	(1.4)	
3a	4	(12.5)	2	(1.4)	
3b	0	(0)	0	(0)	
4a	2	(5.1)	2	(1.4)	
4b	0	(0)	0	(0)	
5	0	(0)	0	(0)	

* Enterotomy during lysis of adhesions; repaired laparoscopically without sequelae.

** Urine leaks resolved spontaneously after stenting.

*** Bleeding resolved spontaneously after transfusion in one patient in each group. One patient in group 1 with platelet dysfunction required reexploration for delayed rupture of a hepatic subcapsular hematoma. One patient in group 2 with normal renal function and a normal contralateral kidney was converted from LPN to open nephrectomy because difficulty to control the hilum with a laparoscopic clamp.

trend toward greater blood loss for larger tumors, although this did not reach statistical significance. Similar to Simmons and cols.⁶, the mean warm ischemia time in our study was longer for larger tumors (22 min vs 17 min; $p = 0.011$), and we did not find a significant difference in complications based on tumor size.

Our postoperative complication rate of 28.1% for tumors > 4 cm is similar to laparoscopic report of 24% and 37%.^{5,6} Four delayed urine leaks occurred on group 1 in which extensive collecting system repair was performed without pre-placement of a ureteral catheter and prior to the adoption of the sliding

Hem-o-lok clip technique. Patients with larger tumors had a relatively greater decline in mean estimated GFR in the short term (Table 4). Possible explanations include a larger amount of tissue resected, longer warm ischemia times, and more parenchymal suturing required to complete the renorrhaphy and achieve hemostasis.

Limitations of our study include the retrospective nature our analysis, and the fact that it analyzes the experience of a single surgeon. Inclusion of different surgeons with varying levels of experience, however, might confound a comparison of outcomes based on tumor size because of the technical

Table 4 - Change in renal function in patients undergoing Laparoscopic Partial Nephrectomy.

	Group 1 (>4 cm) N(19)		Group 2 (≤ 4cm) N(68)		p value
Mean baseline estimated GFR, No. (range)	86.2	(57.3-168.7)	73.5	(37.5-107.0)	0.447
Mean estimated GFR 24 hours after surgery, No. (range)	58.4	(33.3-97.3)	68.9	(37.5-113.5)	0.119
Mean change from baseline in estimated GFR 24 hours after surgery, No. (range)	-13.9	(-102.5 to 64.2)	-4.6	(-30.7 to 32.0)	0.295
Mean estimated GFR (at 1-3 months follow-up), No. (range)	74.0	(33.3-168.7)	76.5	(27.4-126.9)	0.339
Mean change in estimated GFR from baseline (at 1-3 months follow-up), No. (range)	-12.3	(-64.2 to 28.6)	3.0	(-37.3 to 64.8)	0.063

GFR = glomerular filtration rate.

Patients were included if they had preoperative, 24 hour postoperative, and follow-up creatinine 1-3 months after surgery. All values in milliliter per minute per 1.73m².

Table 5 - Pathologic variables for patients who underwent Laparoscopic Partial Nephrectomy.

Characteristic		Group 1(>4 cm)		Group 2(≤ 4cm)		p value
All patients						
Histology, No. (%)	RCC	21	(65.6)	102	(73.4)	0.813
	AML	6	(18.7)	15	(10.8)	-
	Oncocytoma	3	(9.4)	12	(8.6)	-
	Other benign	2	(6.3)	12	(8.6)	-
Pathologic size, cm Mean (range)		5.8	(4.1-9.3)	2.0	(0.8-4.2)	<0.001
PSM No. (%)		1	(3.1)	7	(5.0)	0.360
RCC Patients						
Subtype, No. (%)	Clear cell	12	(57.1)	67	(65.7)	0.360
	Papillary	7	(33.3)	9	(8.8)	-
	Chromophobo	2	(9.6)	26	(25.5)	-
Fuhrman grade, No. (%)	1	0		15	(14.7)	0.267
	2	12	(57)	55	(53.9)	-
	3	9	(42.9)	32	(31.4)	-
	4	0	(0)	0	(0)	-
Pathologic stage, No. (%)	pT1a	4	(19)	91	(89.2)	<0.001
	pT1b	14	(66.7)	0	(0)	-
	pT2	0	(0)	0	(0)	-
	pT3a	3	(14.3)	11	(10.8)	-

RCC= renal cell carcinoma; AML= angiomyolipoma; PSM = positive surgical margins.

challenges of LPN for tumors > 4 cm. The level of experience may influence a surgeon's choice of treatment of renal cell carcinoma (RCC), even as much as tumor size, demographic characteristics, or comorbidities.¹³ The statistical power of our study to detect a difference between groups is limited by

the smaller number of patients with tumors > 4 cm (Table 5). Only early oncologic and functional outcomes are available at this time, and further studies with longer follow-up are needed. Our warm ischemia times were shorter than in comparable laparoscopic series of patients with tumors > 4 cm,

but a potential criticism is that our total operative times were longer. The most important component of the operative time is the warm ischemia time, as this factor affects subsequent renal function. We feel that the investment of additional time for preparation to save even a few minutes of warm ischemia is time well spent. Other explanations for our longer operative times include the fact that many of our patients are obese (mean BMI was 31.6 Kg/m² in group 1 and 30.2 Kg/m² in group 2), and 15.6% of group 1 patients and 25.9% of group 2 patients had undergone prior abdominal surgery.

5. CONCLUSION

In our initial experience, LPN for tumors > 4 cm is safe and feasible, showing comparable outcomes to OPN for smaller tumors, although with longer warm ischemia times. We do not advocate LPN for all patients with renal masses, but it may allow select patients with larger tumors to achieve the convalescence benefits of a minimally invasive approach. Studies with longer follow-up are needed to more definitively evaluate the efficacy of LPN for large tumors.

RESUMO

Introdução: Cirurgia minimamente invasiva por nefrectomia parcial laparoscópica (NPL) normalmente é feita para tumores renais < 4 cm em tamanho. NPL para tumores > 4 cm não tem sido a rotina. **Objetivo:** Para avaliar a segurança e factibilidade da NPL para tumores > 4 cm comparou-se dois grupos de pacientes: um com tumores ≤ 4 cm e outro com tumores > 4 cm. **Materiais e Métodos:** Revisamos dados consecutivos de 171 pacientes que foram submetidos a NPL transperitoneal entre maio de 2002 e maio de 2012 feitas por um mesmo cirurgião. Pacientes foram estratificados em dois grupos: 32 com tumores > 4 cm na imagem pré-operatória (grupo 1) e 139 com tumores ≤ 4 cm (grupo 2). Dados pré-operatórios, perioperatórios, resultados patológicos e funcionais foram analisados e comparados entre os grupos. Usamos o teste X² e student t. O valor $p < 0,05$ foi considerado estatisticamente significativo. **Resultados:** Tamanho médio radiográfico do tumor foi 5,9 cm (4,1 – 9,2) para o grupo 1 e 2,3 cm (0,9 – 4,0) para o grupo 2. Não foi encontrada diferença significativa entre os grupos na perda sanguínea estimada, tempo total da cirurgia, tempo de hospitalização, taxa de complicações e mudança na taxa de filtração glomerular. Pacientes com tumores maiores tem tempo maior de isquemia quente (22 vs 17 min; $p = 0,011$). **Conclusões:** Em nossa experiência, NPL para tumores > 4 cm é segura e factível, mostrando resultados comparáveis a NPL para tumores menores. Mais estudos são necessários para determinar a viabilidade da NPL para tumores maiores como uma forma efetiva de tratamento.

Key words: Laparoscopia. Nefrectomia. Nefrectomia parcial. Carcinoma de células renais.

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