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COMPARATIVE ANALYSIS OF LAPAROSCOPIC VERSUS OPEN PARTIAL NEPHRECTOMY FOR RENAL TUMORS IN 200 PATIENTS

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ABSTRACT

Purpose: Laparoscopic partial nephrectomy is an emerging minimally invasive, nephron sparing approach for renal cell carcinoma. We compared perioperative outcomes after laparoscopic and open nephron sparing surgery (NSS) for patients with a solitary renal tumor of 7 cm or less at a single institution.

Materials and Methods: Since September 1999, 100 consecutive patients have undergone laparoscopic partial nephrectomy for a sporadic single renal tumor of 7 cm or less at our institution. A contemporary cohort of 100 consecutive patients with similar inclusion criteria have undergone open NSS since April 1998. Since our laparoscopic technique was based on our established open surgical principles, the 2 approaches were similar, including transient renal vascular control, sharp tumor excision in a bloodless field, pelvicaliceal repair when necessary, suture ligation of transected intrarenal blood vessels and suture repair of the renal parenchymal defect over a bolster. Demographic, intraoperative, postoperative and short-term followup data were retrospectively compared between the 2 groups.

Results: Median tumor size was 2.8 cm in the laparoscopic group and 3.3 cm in the open group ($p = 0.005$). There were significantly more tumors greater than 4 cm in the open group ($p < 0.001$). There were more patients with a solitary kidney in the open surgical group ($p = 0.002$). More patients in the open group underwent NSS for a malignant tumor ($p = 002$). Comparing the laparoscopic versus open groups, median surgical time was 3 vs 3.9 hours ($p < 0.001$), blood loss was 125 vs 250 ml ($p < 0.001$) and mean warm ischemia time was 27.8 vs 17.5 minutes ($p < 0.001$), respectively. In the laparoscopic and open groups median analgesic requirement was 20.2 vs 252.5 mg morphine sulfate equivalents ($p < 0.001$), hospital stay was 2 vs 5 days ($p < 0.001$) and average convalescence was 4 vs 6 weeks ($p < 0.001$). Median preoperative serum creatinine (1.0 vs 1.0 mg/dl, $p = 0.52$) and postoperative serum creatinine (1.1 vs 1.2 mg/dl, $p = 0.65$) were similar in the 2 groups. No kidney was lost due to warm ischemic injury. Three patients in the laparoscopic group had a positive surgical margin compared to none in the open groups (3% vs 0%, $p = 0.1$). Laparoscopic NSS was associated with a higher rate of major intraoperative complications (5% vs 0%, $p = 0.02$). There were no significant differences in overall postoperative complications, although renal/urological complications were more common in the laparoscopic group (11% vs 2%, $p = 0.01$).

Conclusions: Open surgical partial nephrectomy remains the established standard for nephron sparing treatment of renal tumors. When applied to small renal tumors, the laparoscopic approach is associated with longer warm renal ischemia time, more major intraoperative complications and more postoperative urological complications. Our data also suggest that more deliberate efforts to achieve a wider surgical margin are necessary with the laparoscopic approach. Nevertheless, our data suggest that laparoscopic NSS is emerging as an effective, minimally invasive therapeutic approach with respect to renal functional outcome with the additional advantages of decreased postoperative narcotic use, earlier hospital discharge and a more rapid convalescence. Continued efforts are required to develop laparoscopic renal hypothermia techniques and facilitate intrarenal suturing, while minimizing warm ischemia time.

KEY WORDS: kidney; nephrectomy; laparoscopy; carcinoma, renal cell

Open nephron sparing surgery (NSS) offers long-term preservation of renal function with recurrence-free survival equivalent to that of radical nephrectomy in select patients.[1] Novel energy based, in situ forms of NSS such as cryoablation and radiofrequency ablation have been explored as minimally invasive substitutes for traditional surgical approaches.[2,3] To our knowledge these novel therapies remain developmental and unproven with respect to local cancer control and long-term recurrence-free survival. Recent advances in laparoscopic techniques such as intracorporeal suturing and the availability of laparoscopic vascular instruments have allowed laparoscopic partial nephrectomy to become a viable alternative to open partial nephrectomy, wherein the laparoscopic approach attempts to duplicate traditional, established open surgical techniques.[4] We compared the initial perioperative outcomes of laparoscopic NSS with

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the time tested gold standard results of open NSS at a single institution.

MATERIALS AND METHODS

Inclusion criteria for this single institution retrospective study were patients with a solitary, localized sporadic renal tumor 7 cm or less who were candidates for NSS. The laparoscopic group comprised the initial 100 patients who underwent laparoscopic partial nephrectomy for a renal tumor between September 1999 and January 2002 at our institution. The open surgical group comprised 100 consecutive patients who met study inclusion criteria and underwent open partial nephrectomy from April 1998 through May 2001. All laparoscopic procedures were performed by 1 staff surgeon (ISG) and all open procedures were directed by another staff surgeon (ACN). The techniques for these operations have been previously described in detail.[4,5] Followup and convalescence data were obtained by telephone contact or patient completed questionnaires. Analgesic requirements were calculated by adding the total narcotic requirement during hospitalization normalized to morphine sulfate. Tumor size is reported as the longest single dimension of the lesion, as measured by the pathologist. Central tumors are defined as those extending to the renal sinus, while peripheral tumors did not contact the renal sinus fat. Tumor grade was determined according to the method of Fuhrman et al.[6] Pathological tumor staging was performed according to the TNM system, as modified by Guinan et al, in which tumors less than 4 cm are classified as T1a and tumors 4 to 7 cm are classified as T1b.[7]

Preoperatively all patients were evaluated with a medical history, physical examination, urinalysis, chest x-ray and laboratory studies, including serum creatinine determinations. Spiral computerized tomography scanning with volume rendered 3-dimensional reconstruction was performed in all patients to allow precise intraoperative surgical planning.[8] Postoperatively all patients underwent serum creatinine measurements and excretory urography approximately 4 weeks after surgery. Patients with a serum creatinine above 2.5 mg/dl frequently underwent other imaging studies postoperatively, such as nuclear renography, ultrasonography or magnetic resonance imaging. For study purposes postoperative outcomes were indexed from the time of recovery to postoperative day 30.

Statistical comparisons between laparoscopic and open procedures were made using baseline factors, and intraoperative and postoperative outcomes. Comparisons of continuous variables were made using the Student t or Wilcoxon rank sum test. Summary statistics for these variables are presented as median and quartiles (25th [Q1] and 75th [Q3] percentiles) when the Wilcoxon test was used, and as the mean ± SD when the t test was used. Comparisons of categorical variables were made using Pearson's chi-square or the unconditional exact test. Pairwise comparisons were made between groups using the Dunn, Tukey and Bonferroni multiple comparisons. For determining serum creatinine outcomes in patients with a solitary kidney a comparison of the change from baseline on postoperative day 1 and the last measurement within 30 days was made. In addition, the outcome in the difference between the natural log of preoperative creatinine and the natural log of followup creatinine was used since the latter was not normally distributed. Repeated measures analysis modeling of this difference as a function of time was used as well as assessment of the differences in surgical groups overall and with time. Multivariable analyses were performed on the relationship between continuous outcomes and the surgical approach to adjust for potential confounders. The log transform was used to normalize these outcomes when necessary. The Breslow-Day test for homogeneity of ORs was used to assess the interaction between the type of approach and tumor characteristics for adverse outcomes. All tests were 2-tailed with significance at 0.05 for each hypothesis. Computer software was used for all analyses.

RESULTS

Table 1 lists baseline demographics for the 2 groups. Patients in the laparoscopic group were older ($p < 0.001$), and had smaller tumors ($p = 0.005$). There were more patients with tumors greater than 4 cm in the open group (27 vs 9, $p < 0.001$). While there was no significant difference in the proportion of patients with elective and imperative indications for surgery in the 2 groups ($p = 0.06$), there were more patients with a solitary kidney in the open surgical group ($p = 0.002$). Preoperative serum creatinine was similar in the 2 groups ($p = 0.52$) and no differences were found between the groups in terms of gender ($p = 0.19$), body mass index ($p = 0.64$), side of the tumor ($p = 0.09$) or tumor depth ($p = 0.83$). Clinical stage of all 200 tumors in this study was T1a-b N0 M0-1. A patient in the laparoscopic group had a previously resected solitary metastasis and no evidence of disease other than the primary renal tumor.

Table 2 lists intraoperative and postoperative data. Ice slush was used to achieve renal surface hypothermia in 1 patient in the laparoscopic group and 4 in the open group ($p = 0.99$). Intraoperative ultrasonography was done in 76% of laparoscopic and 15% of open cases. The rates of renal vascular clamping were similar between the 2 groups with

TABLE 1. *Baseline demographics on laparoscopic vs open partial nephrectomy for renal tumor*

	Laparoscopic	Open	p Value
Mean age (SD)	65.1 (11.4)	58.8 (11.6)	<0.001 (Student t test)
Median body mass index (Q1, Q3)	28.0 (25, 34)	28.1 (25, 30)	0.64 (Wilcoxon rank sum test)
Median American Society of Anesthesiologists score (Q1, Q3)	3.0 (2, 3)	3.0 (3, 3)	0.06 (Wilcoxon rank sum test)
Median mg/dl preop serum creatinine (Q1, Q3)	1.0 (1, 1)	1.0 (1, 1)	0.52 (Wilcoxon rank sum test)
Tumor size (cm):	2.8 (2, 4)	3.3 (3, 4)	0.005 (Wilcoxon rank sum test)
Median (Q1, Q3)			
% 4 or Less	91	73	<0.001 (Wilcoxon rank sum test)
% Greater than 4	9	27	
% Men/women	58/42	67/33	0.19 (Pearson chi-square test)
% NSS indications/contralat kidney status:			0.06 (Pearson chi-square test)
Elective/normal	59	46	0.002*
Imperative compromised	41	54	
	33	26	
Imperative absent	8	28	
% Tumor side:			0.09 (Pearson chi-square test)
Lt	42	54	
Rt	58	46	
% Tumor depth:			0.83 (Pearson chi-square test)
Central	34	33	
Peripheral	66	67	

* Using 3 categories (normal, compromised or absent contralateral kidney).

TABLE 2. *Intraoperative and postoperative data*

	No. Pts	Laparoscopic	No. Pts	Open
		Intraop		
Mean warm ischemia mins (SD)	95	27.8 (7.7)	92	17.5 (8.2)
% Renal vessel clamping:				
Artery & vein	88	93.6	87	90.6
Artery only	3	3.2	6	6.3
Neither artery nor vein	3	3.2	3	3.1
% Repair pelvicaliceal system:				
No	35	36.1	17	26.6
Yes	62	63.9	47	73.4
Median ml estimated blood loss (Q1, Q3)	100	125.0 (100, 200)	76	250.0 (150, 400)
Median mins total operative time (Q1, Q3)	98	180.0 (150, 210)	100	231.5 (198, 264)
% Complications	100	5	100	0
		Postop		
Median mg MSO_4 equivalent (Q1, Q3)	76	20.2 (13, 33)	54	252.5 (143, 341)
Median days hospital stay (Q1, Q3)	97	2.0 (2, 3)	98	5.0 (5, 7)
Median wks complete convalescence (Q1, Q3)	66	4.0 (3, 6)	62	6.0 (4, 10)
% Complications	100	16	100	13

The renal parenchyma was sutured in all patients intraoperatively.

the renal artery and vein clamped ($p = 0.6$) and renal parenchymal reconstruction in the majority of cases (table 2). Notable findings include longer warm ischemia time in the laparoscopic group, shorter total surgical time, less blood loss, decreased narcotic analgesic requirement, a shorter hospital stay and more rapid convalescence (all $p < 0.001$).

The laparoscopic group had a 5% incidence of major intraoperative complications vs 0% in the open group, which was statistically significant ($p = 0.03$). Intraoperative complications consisted of renal parenchymal hemorrhage (1,000 to 1,500 cc) in 3 patients, which was controlled laparoscopically. Likely causes of hemorrhage were an unoccluded renal artery in the setting of multiple vessels and suboptimal placement of a laparoscopic bulldog clamp. Ureteral injury occurred in 1 patient with 3 renal arteries in whom the ureter and lower pole accessory artery were adherent to an exophytic lower pole tumor and the ureter was inadvertently resected. An ileal ureter was created laparoscopically using intracorporeal techniques at the same operative session. Postoperatively this patient had bowel leakage from the enteric anastomosis and required laparotomy and revision of the anastomosis. Another patient sustained a slight, superficial bowel laceration during port site closure, which was repaired laparoscopically with no further sequelae. All 100 laparoscopic procedures were completed without open conversion.

There was no difference in the overall incidence of postoperative complications between the 2 groups (16% vs 13%, $p = 0.55$, table 3). However, the incidence of major intraoperative and postoperative renal/urological complications was significantly greater in the laparoscopic than in the open group ($p = 0.01$, table 4). Intraoperative urological complications in the laparoscopic group occurred in 4 patients, as described. Postoperative urological complications developed in the laparoscopic group in an additional 7 patients. Three patients had urine leakage, which subsided spontaneously within 2 weeks in 1, while 2 required ureteral stenting with percutaneous computerized tomography guided aspiration of a urinoma. Three had renal hemorrhage or a perirenal hematoma. One case was successfully managed by supportive measures only and 1 was managed by percutaneous embolization of a peripheral bleeding vessel. A patient with a solitary kidney had secondary hemorrhage 5 days postoperatively and ultimately required nephrectomy. In addition, 1 patient had gross hematuria postoperatively, which subsided spontaneously with bed rest. In the open group 1 patient had presumptive urine leakage, which resolved spontaneously. An additional patient in the open group had ureteropelvic junction obstruction of the ipsilateral kidney, which was managed successfully by retrograde balloon dilation.

TABLE 4. *Renal/urological complications of laparoscopic and open partial nephrectomy*

	No. Laparoscopic	No. Open
Intraop:		
Renal hemorrhage	3	0
Ureteral resection	1	0
Postop:		
Urine leakage	3	1
Perirenal hematoma	1	0
Renal hemorrhage, embolization	1	0
Renal hemorrhage, nephrectomy	1	0
Hematuria	1	0
Ureteropelvic obstruction	0	1
Totals	11	2

Histopathology confirmed the diagnosis of renal cell carcinoma (RCC) in 70 laparoscopic and 85 open cases ($p = 0.002$) with the majority being stage pT1a (all stages $p = 0.48$) and grade 2 (all grades $p = 0.33$, table 5). The groups did not differ in median parenchymal margin width ($p = 0.11$) or median specimen weight ($p = 0.53$). By stringent definition a positive surgical margin was present in 3 laparoscopic and no

TABLE 3. *Overall complications after laparoscopic and open partial nephrectomy*

	% Laparoscopic	% Open	p Value
Complications:			
Intraop	5	0	0.03 (unconditional exact test)
Postop	16	13	0.55 (Pearson chi-square test)
Total No. complications:	19	13	
1	15	12	
2	4	1	
Wound	3	1	
Pulmonary	2	0	
Cardiovascular	3	6	
Gastrointestinal	3	3	
Thrombotic	1	1	
Renal/urological	7	2	

TABLE 5. *Histopathology results of laparoscopic vs open partial nephrectomy for renal tumor*

	Laparoscopic	Open	p Value
% Pathological diagnosis:			0.01 (Pearson chi-square test)
RCC	70.0	85.0	
Benign	30.0	15.0	
% RCC:	70.0	85.0	0.002 (Fisher exact test)
Clear cell	51.4	77.6	
Papillary	35.7	12.9	
Other	12.8	9.4	
% Benign:	30.0	15.0	0.052 (Fisher exact test)
Oncocytoma	43.3	86.7	
Cyst	10.0	0.00	
Angiomyolipoma	23.3	6.7	
Other	0.0	6.7	
% T stage:			0.48 (Wilcoxon rank sum test)
pT1a	84.1	79.3	
pT1b	10.1	14.9	
pT3a	5.8	5.8	
% Grade:			0.33 (Wilcoxon rank sum test)
I	12.3	11.0	
II	61.5	56.1	
III	24.6	25.6	
IV	1.5	7.3	
% Margin:			0.1 (Fisher's exact test)
Neg	97	100	
Pos	3	1	
Median mm margin distance (Q1, Q3)	4.0 (2, 7)	4.0 (2, 5)	0.11 (Wilcoxon rank sum test)
Median gm specimen wt (Q1, Q3)	29 (17, 50)	29 (12, 53)	0.53 (Wilcoxon rank sum test)

open case (p = 0.1). Of the 3 laparoscopic cases with a positive surgical margin 1 was oncocytoma and 2 were RCC. All 3 cases occurred within the first 50 laparoscopic partial nephrectomies. In the 2 patients with RCC and a positive surgical margin postoperative radiographic followup at 2 and 3 years, respectively, showed no evidence of local or systemic disease recurrence.

All kidneys functioned postoperatively except 1 removed for postoperative hemorrhage in the laparoscopic group. Overall postoperative serum creatinine was not significantly different between the laparoscopic and open groups (1.1 vs 1.2 mg/dl, p = 0.65). To evaluate more accurately the effects of surgical technique on renal function we examined serum creatinine results in patients with a solitary kidney (table 6). Analysis of serum creatinine on postoperative day 1 and the last serum creatinine value within 30 days were not different in the 2 groups (p = 0.48 and 0.21, respectively). Also, on repeated measures analysis of the natural log difference in serum creatinine as a function of time on extended followup (greater than 30 days) a parallel time-course relationship was found without any significant differences between the open and laparoscopic groups (p = 0.11).

DISCUSSION

Prior worldwide single-institution experience with laparoscopic partial nephrectomy has been reported in 74 patients,[9–16] not including an initial report from our group.[4] In the current study we expanded our experience and retrospectively compared the perioperative outcomes of our initial 100 laparoscopic cases with a consecutive contemporary series of 100 cases of open NSS. We believe that an interim critical appraisal of the new laparoscopic approach is important to evaluate its current status compared with that of contemporary open surgery.

Several notable findings in this study deserve mention. The laparoscopic approach was associated with a higher rate of intraoperative complications (5% vs 0, p = 0.03) and a higher overall rate of renal/urological complications (11% vs 2%, p = 0.01), of which the most common were renal hemorrhagic sequelae. Perhaps it was due to gradual expansion of our eligibility criteria for laparoscopic NSS to include some patients with central and more deeply infiltrating tumors. However, statistical analysis failed to demonstrate a relationship between such cases and operative morbidity. A more likely explanation is the fact that open NSS enables more precise and rapid placement of as many parenchymal sutures as needed to achieve complete hemostasis. The limitations of time and precision with laparoscopic suturing do not currently allow this maneuver to be done with comparable efficacy. The best management of post-resection parenchymal hemorrhage is preventive through well functioning vascular instruments for hilar control and meticulous oversewing of transected vessels within time limits that do not incur ischemic renal damage. Intraoperative renal parenchymal hemorrhage represents a difficult management dilemma during partial nephrectomy, particularly during laparoscopic NSS. Hilar re-clamping is generally not performed because it may increase renal susceptibility to calcium mediated reperfusion injury.[17, 18] While placement of sutures in a reperfused kidney is sometimes necessary, it risks parenchymal tearing and added bleeding.

This study highlights the technical feasibility and emerging benefits of laparoscopic partial nephrectomy in properly selected patients with a single small renal tumor. The bene-

TABLE 6. *Renal functional outcome in patients with solitary kidney*

	Laparoscopic (7 pts)	No. Pts	Open
Median mg/dl baseline creatinine (Q1, Q3)	1.1 (0.9, 1.2)	27	1.2 (0.9, 1.4)
Mean postop day 1 mg/dl creatinine (SD)	1.7 (0.61)	23	1.7 (0.58)
Mean mg/dl last creatinine within 30 days (SD)	1.7 (0.70)	27	1.5 (0.52)
Mean postop day 1 creatinine difference (SD)*	0.66 (0.61)	22	0.48 (0.37)
Mean mg/dl difference in last creatinine within 30 days (Q1, Q3)†	0.50 (0.0, 1.4)	26	0.20 (0.0, 0.4)
Mean change within 30 days/followup days (Q1, Q3)	0.07 (0.0, 0.3)	26	0.03 (0.0, 0.1)

* Postoperative day 1 minus baseline creatinine.

† Last creatinine within 30 days minus baseline creatinine.

fits of laparoscopic NSS include less narcotic requirement for pain, a shorter hospital stay and a more rapid recovery with satisfactory preservation of renal function. Open NSS is an established approach with proven long-term efficacy that enables efficient in situ renal preservation and complex renal reconstruction following the excision of large, central or multiple tumors.

The laparoscopic and open approaches are also associated with specific disadvantages. The disadvantages of the open approach include a greater need for narcotic analgesics to control pain, a longer hospital stay and longer convalescence. Patients undergoing laparoscopic NSS are at higher risk for a renal or urological complication. Although most of the latter complications can be managed successfully without the need for surgical intervention, 1 solitary kidney was lost in the laparoscopic group due to postoperative hemorrhage. Our data also suggest that more deliberate efforts to achieve a wider surgical margin at surgery are necessary with the laparoscopic approach. The limited angulation of laparoscopic instruments tends to decrease the width of the margin as one dissects more deeply into the parenchyma. In addition, trying to attain wider margins laparascopically after initiating the parenchymal incision is technically difficult. Thus, an initial wider margin of resection is critically important and necessary during laparoscopic partial nephrectomy.

It is appropriate to acknowledge some limitations of this study. An inherent limitation is the retrospective analysis used. Several important parameters differed significantly between the 2 groups. The open group may have been at higher risk for surgical therapy since there were significantly more patients with larger tumors, malignant tumors and a solitary kidney. The mean age of patients in the laparoscopic group was greater. Some of these differences may have impacted our results, although due to small sample sizes within subgroups there may not have been sufficient statistical power to detect important associations.

Our aggregate experience with major laparoscopic urological surgery now encompasses more than 1,300 adrenal, kidney, bladder and prostate operations. In this context we wish to emphasize that laparoscopic partial nephrectomy is a challenging technique, which in our view represents the technical epitome of advanced laparoscopic urological surgery. At this time laparoscopic partial nephrectomy should be limited to patients with a single small renal tumor with open partial nephrectomy remaining the standard of care for more complex conditions.

CONCLUSIONS

Laparoscopic partial nephrectomy is technically feasible in select patients with a single small renal tumor. Laparoscopic NSS is associated with less postoperative analgesic requirement, earlier hospital discharge and more rapid convalescence. Technical factors, such as more tedious and inefficient suturing of the transected renal parenchyma, are likely contributors to an increased rate of renal and urological complications. Continued efforts are needed to develop laparoscopic renal hypothermia techniques and facilitate intrarenal hemostasis, while minimizing warm ischemia time. Laparoscopic partial nephrectomy is an advanced technique that should be performed by surgeons with considerable laparoscopic expertise at centers where close interaction exists between open and laparoscopic surgeons.

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