นิพนธ์ต้นฉบับ

Laparoscopic Versus Open Radical Nephrectomy for Renal Cell Carcinoma: Oncologic and Short-term Clinical Outcomes in Phramongkutklao Hospital

Satit Siriboonrid, M.D.

Abstract

Background: Laparoscopic surgery for renal cell carcinoma is a recognized treatment modality. The advantage of the laparoscopic procedure include better visualization of critical structures such as blood vessels (renal artery and renal vein) and surrounding organs, less tissue trauma and blood loss, less post operative pain, earlier operative recovery and shorter hospital stay. The objective of this study was to review and compare short-term oncologic as well as various perioperative outcome between laparoscopic and open surgery for renal cell carcinoma, as performed by one surgeon at Phramongkutklao hospital.

Method: Medical records of and pathologic findings in patients with renal cell carcinoma treated by one surgeon (Satit Siriboonrid, MD) during the period from June 2007 to June 2010 were reviewed. Baseline data, radiologic results, tumor characteristics, operative findings and follow-up data were abstracted from the records. Renal cell carcinoma staging was according to the American joint Committee on Cancer, 2002.

Result: During the period between June 2007 and June 2010, 145 patients fulfilling the inclusion criteria were operated on for renal cell carcinoma by one surgeon. Of these, 75 (51.7%) underwent laparoscopic radical nephrectomy and 70 (48.3%) underwent open radical nephrectomy. No significant difference could be detected in basic data. Laparoscopic surgery was associated with longer operative time than open surgery, although there was less blood loss. Pathologic examination of the resected specimens did not reveal any statistically or clinically significant differences between the two groups in terms of tumor-free margins and tumor grade. The occurrence of postoperative complications, including infectious complications, was not clearly different between the two groups of patients. The amount of postoperative morphine required for pain was significantly less in the laparoscopic group. The delay bowel movement or oral diet was also significantly less for the laparoscopic group.

Conclusion: There was no evidence of any significant difference between laparoscopic and open surgery for patient with renal cell carcinoma in the term of operative and early oncologic outcomes in the present study. More patients need to be included in a future analysis. Further long-term follow-up is still warranted to confirm or refute the present finding.

Key words: Laparoscopic radical nephrectomy, Open radical nephrectomy, renal cell carcinoma, Oncologic and Short-term clinical outcomes

Division of urology, Department of surgery, Phramongkutklao Hospital and Phramongkutklao College of Medicine

Introduction

Laparoscopic surgery for renal cell carcinoma is a recognized treatment modality. In the decade since it introduction in 1991[1], laparoscopic surgery has been shown to be a viable alternative to open surgery for renal cell carcinoma. The advantage of the laparoscopic procedure include better visualization of critical structures such as blood vessels (renal artery and renal vein) and surrounding organs, less tissue trauma and blood loss, less post operative pain, earlier operative recovery and shorter hospital stay[2]. However, concerns regarding the laparoscopic procedure centered on the adequacy of cancer removal and hence on cancer-related survival or disease-free survival, or "oncologic" outcome. Short and medium-term follow up for oncologic outcomes based on several randomized clinical trials have not show any clear difference between the laparoscopic and open procedure[3]. Long-term outcomes of larger trials are becoming available and, similarly, do not seem to show significant differences[4]. The objective of this study was to review and compare short-term oncologic as well as various peri-operative outcome between laparoscopic and open surgery for renal cell carcinoma, as performed by one surgeon at Phramongkutklao hospital.

Patients and Methods

Medical records of and pathologic findings in patients with renal cell carcinoma treated by one surgeon (Satit Siriboonrid, MD) during the period from June 2007 to June 2010 were reviewed. The study was approved by the Phramongkutklao hospital's research ethics committee. Patients in the last years usually underwent laparascopic surgery, while open surgery was mainly done in the earlier period. Baseline data, radiologic results, tumor characteristics, operative findings and follow-up data were abstracted from the records. Renal cell carcinoma staging was according to the American joint Committee on Cancer, 2002.

Patients were included in the study if they had renal cell carcinoma and had undergone radical nephrectomy. Patients were excluded if they had severe medical co-morbidities. All patients were given preoperative light mechanical bowel preparation. Preoperative prophylactic antibiotics were given 30 minutes prior to induction of general anesthesia, and continued until 24 hours after operation.

Both open and laparoscopic operations were performed according to standard procedures. At each tumor location, the attempted extent of resection was the same for both groups. For laparoscopic radical nephrectomy, 3 ports were used (10 mm. at umbilicus and two of 5 mm. ports as intraperitoneal laparoscopic radical nephrectomy fashion). After pneumoperitoneum was achieved the abdominal cavity was explored, white line of Toldt was mobilized and important structures were identified and vascular pedicles were controlled with laparoscopic vascular stapling instrument. Ureter was controlled with silver clip 10 mm. Endobag was used for removing whole specimen via extended 10 mm. port. For open approach, anterior subcostal incision was used and radical nephrectomy was done as intraperitoneal approach fashion. We preferred open approach in mass size beyond 10 cm in diameter and patient who had ASA class 2 or 3.

Nasogastric tube were retained in all patients postoperatively. The criteria for removing nasogastric tube were the same in both groups of patients (gastric content less than 100 cc. per day and absence of significant abdominal distension), and oral feeding was resumed after active bowel sound.

Continuous variables were summarized as mean (SD) or median (range) as appropriate. Categorical variables were summarized as counts and percen-

tages. Continuous variables were contrasted between treatment groups (type of surgery) using independent sample t-test or Wilcoxon rank-sum test as appropriate, and categorical variables were contrasted using Fisher's exact test or chi-square test as appropriate. All statistical analyses were performed with Stata v.9 software (State Corp, College Station, TX, USA). Significant p-values were defined as values 0.05 or less.

Results

During the period between June 2007 and June 2010, 145 patients fulfilling the inclusion criteria were operated on for renal cell carcinoma by one surgeon (Satit Siriboonrid, MD). Of these, 75 (51.7%) underwent laparoscopic radical nephrectomy and 70 (48.3%) underwent open radical nephrectomy. Baseline clinical and pathologic characteristics of patients in both groups are presented in Table 1. No significant difference could be detected between the two groups terms of age, gender, height, comorbid disease, previous surgery, clinical findings, American Society of Anesthesiologist (ASA) class, and radiologic investigation. TMN stage and Lactase dehydrogenase enzyme (LDH) levels were also similar between the two groups. There was no significant difference in term of tumor location and size. The other findings of symptoms were fever in 3 patients from both groups. In physical findings, other findings were 1 case of fever, 2 cases of pale conjunctivae and 1 case of icteric sclera in laparoscopic group and 3 cases of pale conjunctivae in open group.

Laparoscopic surgery was associated with longer operative time (average: 201 minutes) than open surgery (average 152 minutes), although there was less blood loss (median blood loss of 100 mL. compared with 200 mL. for open surgery), as may be expected (Table 2). Vascular stapling instruments were used for patients in the laparoscopic group. Three patients in laparoscopic group (4%) was converted to open surgery because of the tumor attachment to the duodenum.

Pathologic examination of the resected specimens did not reveal any statistically or clinically significant differences between the two groups in terms of tumor-free margins and tumor grade (Table 3).

But the larger tumor (tumor size in diameter >10 cm.) was done in open fashion more than laparoscopic fashion ($p<0.001$).

The occurrence of postoperative complications, including infectious complications, was not clearly different between the two groups of patients (Table 4). 1 patients of open group had surgical site infection and others had fever. In laparoscopic group, 2 patients had right scapular pain, 3 patients had fever and 4 patients had subcutaneous emphysema. The amount of postoperative morphine required for pain was significantly less in the laparoscopic group. The delay bowel movement or oral diet was also significantly less for the laparoscopic group. However the length of hospital stay was not significantly different between two groups. There were no operative deaths or tumor recurrence in either of two groups.

Discussion

The present study confirmed previous studies that the result of laparoscopic surgery for renal cell carcinoma in terms of extent of resection and operative complications are comparable to those of the open procedure.[5] The advantages including less severe postoperative pain and earlier bowel function recovery, for laparoscopic procedure, were observed in the present study as well. Many randomized controlled trials (RCT)[6], as well as non-randomized observational studies[7], have been conducted recently to compare the safety and effectiveness of laparoscopic surgery with those of open surgery for

Table 1 *Characteristics of each group*

Characteristics	Open surgery* (70)	Laparoscopic surgery* (75)	p-value**
Age (years): mean (SD)	60.4 (11.6)	58.4 (14.4)	0.504
Gender:men (%)	41 (58)	46 (61)	0.797
Height (cm.): mean (SD)	161.8 (8.4)	162.5 (8.1)	0.727
Weight (kg.): mean (SD)	55.7 (9.5)	58.3 (10.4)	0.232
Hypertension (%)	13 (19)	19 (25)	0.490
DM (%)	7 (10)	17 (22)	0.139
Previous surgery (%)	11 (15)	14 (19)	0.554
Alcohol consumption (%)	15 (21)	17 (22)	0.825
Smoking (%)	11 (17)	17 (22)	0.521
Symptoms			
- Abdominal or flank mass	2 (2.9)	1 (1.3)	0.693
- Flank pain	5 (7.1)	4 (5.3)	0.554
- Gross hematuria	4 (5.7)	3 (4)	0.734
- Microscpic hematuria	6 (8.6)	5 (6.7)	0.683
- Incidental finding	52 (74.3)	60 (80)	0.547
- Other causes (as result)	1 (1.4)	2 (2.7)	0.072
Physical finding			
- Abdominal or flank mass	2 (2.9)	1 (1.3)	0.072
- Other findings (as result)	4 (5.7)	3 (4)	0.734
ASA class			
- 1	49 (71)	59 (78)	0.500
- 2	19 (27)		
- 3	1 (2)		
Preoperative CT (yes)	70 (100)	75 (100)	
Tumor location			
- Right upper pole	8 (11.4)	7 (9.3)	0.139
- Right middle pole	25 (35.7)	30 (40)	0.138
- Right lower pole	5 (7.1)	4 (5.3)	0.073
- Left upper pole	12 (17.1)	18 (24)	0.684
- Left middle pole	15 (21.4)	12 (16)	0.690
- Left lower pole	5 (7.1)	4 (5.3)	0.073
Size of tumor in diameter (cm.)			
- < 4 cm.	13 (18.6)	19 (25.3)	0.687
- 4-7 cm.	22 (31.4)	24 (32)	0.678
- 7-10 cm.	21 (30)	30 (40)	0.500
- >10 cm.	14 (20)	2 (2.6)	<0.001
LDH. Level: median (range)	405 (240-680)	396 (230-700)	0.453
TNM stage			
Stage I	25 (35.7)	32 (42.7)	0.546
Stage II	45 (64.3)	43 (57.3)	0.653
Stage III	0	0	
Stage IV	0	0	

* summary statistic is number (%) unless stated otherwise

** p-value by chi-square test, Fisher's exact test, t-test and rank as appropriate

Table 2 *Intraoperative findings*

	Open surgery* (n=70)	Lap surgery* (n=75)	p-value**
Operative time (min.): mean (min.) (SD)	152 (±20)	201(±27)	<0.001
Blood loss (ml.): mean (range)	200 (50-700)	100 (10-500)	<0.001
Intraabdominal adhesions	4 (5.7)	3 (4)	0.741
Intraoperative complications	0	0	

* summary statistic is number (%) unless stated otherwise

** p-value by chi-square test, Fisher's exact test, t-test and rank as appropriate

Table 3 *pathological findings*

	Open surgery* (n=70)	Lap surgery* (n=75)	p-value**
Tumor grade			
Well differentiated	39 (55.7)	38 (50.7)	0.673
Moderately well differentiated	29 (41.4)	33 (44)	
Poorly differentiated	2 (2.9)	4 (5.3)	
Free margin in all parts of specimen	70 (100)	75 (100)	

* summary statistic is number (%) unless stated otherwise

** p-value by chi-square test, Fisher's exact test, t-test and rank as appropriate

patients with renal cell carcinoma. All results, whether short-term (less than 5 years) or longer term, have not revealed any significant differences between the two procedures in terms of oncologic outcome such as the adequacy of tumor resection, lymph node harvest and overall survival or disease-free survival. The benefit of the laparoscopic procedure, including less postoperative pain and earlier functional recovery as demonstrated in present study, were clearly shown in all studies. Port site or incision wound recurrences were rare, or at least equivalent to open surgery[8]. Intraoperative blood loss was usually considerably less than in open approach, and the excellent visualization contributed to such good outcomes. Although an increase in operative time can be seen in all studies, this increase tends to be much less as the operator becomes more expe-rienced with the procedure. In the present study, after the learning curve period (20 cases in this study), the operative time was usually less than one hour longer for the laparoscopic procedure compared with the open procedure.

Studies addressing the quality of life after laparoscopic as compared with open surgery did not show any appreciable differences, although there was a tendency for a better quality of life in patients undergoing laparoscopic surgery, especially during the early postoperative period (up to 4 weeks)[9]. Duration of retaining NG tube in laparoscopic group prolonged because some patients was received

Table 4 *Postoperative and short-term outcome*

Finding	Open surgery* (n=70)	Lap surgery* (n=75)	p-value**
Postoperative complications (as result)	7 (10)	9 (12)	0.229
Postoperative IV morphine within 24 hrs	51 (73)	33 (44)	0.008
Acetaminophen usage in postoperative time	24 (34)	5 (6)	<0.001
Days on NG tube: median (range)	3 (0-10)	2 (1-4)	0.012
Days on urinary catheter: median (range)	2.5 (0-7)	2 (1-8)	0.510
Days on abdominal drains: median (range)	5 (0-14)	5 (0-20)	0.860
Days till bowel movement: median (range)	4 (1-8)	2 (1-4)	<0.001
Days till oral diet: median (range)	5 (2-10)	3 (2-6)	<0.001
Surgical site infection	1 (1.4)	0	0.009
Length of hospital stay (days): median (range)	11 (9.26)	10 (7-14)	0.258
Death at last follow-up	0	0	
Recurrence at last follow-up	0	0	
Port site recurrence (laparoscopic group)		0	
Follow-up time (months): median (range)	12 (1-48)	7.5 (1-44)	0.002

* summary statistic is number (%) unless stated otherwise

** p-value by chi-square test, Fisher's exact test, t-test and rank as appropriate

inadequate light mechanical bowel preparation and poor compliance for this regimen. According to some studies, the cost of laparoscopic procedure compared favorably with the open procedure, because the expense of laparoscopic instruments was partially offset by the savings and economic output associated with shorter hospital stay and earlier return to work, as well as a better quality of life,[10] but not all studies agree[11]. In my hospital, patients pay nothing in open procedure (government support) and pay more than 20,000 bath in laparoscopic surgery. These economic analyses, done from the viewpoint of developed countries, might not apply to other countries such as Thailand where the cost of laparoscopic surgery overwhelms the cost of open surgery and saving related to shorter hospital stay.

Reason for the conversion from laparoscopic to open surgery are usually related to locally advanced cancer, inadequate visualization of critical structure and adhesion[12]. The conversion rate of 3% in the present study is rather low, but this number is unreliable because of the small sample size. In converted cases, preoperative radiographs showed plan for dissection but can not dissect in field because of severe adhesion. Preoperative radiologic evaluation of the primary tumor and evidence of previous, extensive surgery can be used to select appropriate patients for laparoscopic surgery, and in the process reduce the risk of conversion.

Conclusions

There was no evidence of any significant difference between laparoscopic and open surgery for patient with renal cell carcinoma in the term of operative and early oncologic outcomes in the present study. More patients need to be included in a future analysis. Further long-term follow-up is still warranted to confirm or refute the present finding.

เอกสารอ้างอิง

1. Clayman RV, Kavoussi LR, Soper NJ, Dierks SM, Meretyk S, Darcy MD, et al. Laparoscopic nephrectomy: Initial case report. **J Urol** 1991; 146:278-82.
2. Clayman RV, Kavoussi LR, McDougall EM, Soper NJ, Figenshau RS, Chandhoke PS, et al. Laparoscopic nephrectomy: A review of 16 cases. **Surg Laparosc Endosc** 1992; 2:29-34.
3. Cadeddu JA, Ono Y, Clayman RV, Barrett PH, Janetschek G, Fentie DD, Laparoscopic nephrectomy for renal cell cancer: evaluation of efficacy and safety: a multicenter experience. **Urology** 1998; 52(5):773-7.
4. Chan DY, Cadeddu JA, Jarrett TW, Marshall FF, Kavoussi LR. Laparoscopic radical nephrectomy: cancer control for renal cell carcinoma. **J Urol** 2001; 166(6):2095-9.
5. Kerbl K, Clayman RV, Mc Dougall E, Kavoussi LR. Laparoscopic nephrectomy: current status. **Arch Esp Urol** 1993; 46(7):581-4.
6. Fahlenkamp D, Rassweiler J, Fornara P, Frede T, Loening SA. Complications of laparoscopic procedures in urology: experience with 2,407 procedures at 4 German centers. **J Urol** 1999; 162(3 Pt 1):765-70.
7. Copcoat MJ, Joyce AJ, Popert R, et al: Laparoscopic nephrectomy the King's experience. Minim Invas Ther 1992; 1(Suppl):67.
8. Shuford MD, McDougall EM, Chang SS, LaFleur BJ, Smith JA Jr, Cookson MS. Complications of contemporary radical nephrectomy: comparison of open vs. laparoscopic approach. **Urol Oncol** 2004; 22(2):121-6.
9. Varkarakis I, Neururer R, Harabayashi T, Bartsch G, Peschel R. Laparoscopic radical nephrectomy in the elderly. **BJU Int** 2004 Sep; 94(4):517-20.
10. Rassweiler JJ, Stock C, Frede T, Seemann O, Henkel T, Alken P. Transperitoneal and retroperitoneal laparoscopic nephrectomy in comparison with conventional nephrectomy. **Urologe A** 1996; 35(3):215-22.
11. Rassweiler J, Fornara P, Weber M, Janetschek G, Fahlenkamp D, Henkel T, et al. Laparoscopic nephrectomy: the experience of the laparoscopy working group of the German Urologic Association. **J Urol** 1998; 160(1):18-21.
12. Kerbl K, Clayman RV, McDougall EM, Gill IS, Wilson BS, Chandhoke PS, et al. Transperitoneal nephrectomy for benign disease of the kidney: a comparison of laparoscopic and open surgical techniques. **Urology** 1994; 43(5):607-13.