KJU
Korean Journal of Urology

www.kjurology.org
DOI:10.4111/kju.2011.52.7.474

Robotics/Laparoscopy

Laparoscopic versus Open Radical Nephrectomy in T2 Renal Cell Carcinoma: Long-Term Oncologic Outcomes

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Purpose: Laparoscopic radical nephrectomy (LRN) has become the standard technique for radical nephrectomies for T1 renal tumors (7 cm or less). We extended our experience with LRN to T2 renal tumors (greater than 7 cm) and compared the efficacy and long-term oncologic outcomes with those of open radical nephrectomy (ORN) for T2 clear renal cell carcinoma (RCC) in the same period.

Materials and Methods: We retrospectively analyzed the data from 33 patients who underwent LRN and 35 patients who underwent ORN in our institution from January 2003 to June 2006 for T2N0M0 RCC. We compared long-term oncologic outcomes between the two groups.

Results: The median follow-up periods were 60.0 months (range, 48.0-77.0 months) and 65.6 months (range, 56.0-77.0 months) in the LRN and ORN groups, respectively. There were no statistically significant differences between the two groups in the patients' demographic data. There were no significant differences in the 5-year overall survival rate, the cancer-specific survival rate, or the recurrence-free survival rate.

Conclusions: Our results suggest that LRN for the management of T2 RCC is feasible and efficacious and that the long-term oncologic outcomes of LRN are comparable to those of ORN.

Key Words: *Laparoscopy; Nephrectomy; Renal cell carcinoma; Survival*

Article History:
received 25 April, 2011
accepted 31 May, 2011

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This research was supported by Kyungpook National University Research Fund, 2010.

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INTRODUCTION

Since the first series of laparoscopic nephrectomies were introduced in 1991 by Clayman et al [1], laparoscopic radical nephrectomy (LRN) has become the standard technique for radical nephrectomies for T1 renal tumors (7 cm or less), except in favorable cases of nephron-sparing surgery [2,3]. Multiple studies have repeatedly shown the feasibility, the low morbidity, and the excellent oncologic efficacy of LRN [2-9]. However, most of the current literature has focused on LRN for masses that are less than 7 cm, which are now more often treated with nephron-sparing surgery. Although the indications for LRN are being expanded to include masses larger than previously indicated, the literature to date lacks studies addressing the long-term outcomes of laparoscopic nephrectomy for masses greater than 7 cm, although several recent publications have reported on surgical outcomes [10-13]. Moreover, there are currently no reports on the long-term oncologic outcomes of LRN for T2 renal tumors in Korea.

We retrospectively evaluated patients undergoing LRN for large tumors (greater than 7 cm) at our center and compared their long-term oncologic outcomes with those from a similar cohort of patients undergoing open radical nephrectomy (ORN) during the same period.

MATERIALS AND METHODS

From January 2003 to June 2006, 68 patients underwent radical nephrectomy for T2 renal cell carcinoma (RCC) (33 LRN and 35 ORN). The choice of surgical procedure was based on referrals and surgeon preference. All cases were pathologically confirmed as clear cell carcinoma. Patients with T3-stage, T4-stage, or metastatic disease were exclud-

ed. Study participants were followed up for at least 48 months.

The demographic parameters included age, body mass index (BMI), gender, and tumor laterality. The pathologic data included tumor size and grade (Fuhrman's nuclear grading system). To evaluate operative outcomes, we compared operative time, actual blood loss (ABL) [14], the transfusion rate, and the complication rate. To analyze the oncologic outcomes, we compared 5-year overall survival, recurrence-free survival, and cancer-specific survival.

The preoperative diagnosis and the clinical stage were based on contrast-enhanced computed tomography (CT) of the abdomen. All patients were examined with chest CT and a bone scan to confirm distant metastasis. Our follow-up protocol consisted of a physical examination, chest-abdomen CT, and a complete metabolic profile every 6 months.

ORN was performed through either a flank or a subcostal incision. Subcutaneous tissue and abdominal muscle were dissected and divided. After blunt dissection of the pararenal space to mobilize the kidney, the peritoneum was incised, and the posterior peritoneum and Gerota's fascia were divided. On approach to the hilar area, the renal artery was clamped. The renal vein and ureter were ligated and cut, and then the renal artery was ligated and cut. We extracted the kidney, which was surrounded by perinephric fat and enveloped by Gerota's fascia, while maintaining the position of the Jackson-Pratt drain at the renal fossa. Para-aortic or paracaval and hilar lymph node dissection (LND) were performed when an enlarged lymph node was found radiologically before surgery or grossly during the operation.

LRN was performed by use of the transperitoneal approach in all cases. Pneumoperitoneum was achieved by using a Veress needle, and 3 or 4 ports were placed depending on the case. After laterocolic incision and mobilization of the colon, the renal hilum was dissected in the standard fashion with adequate visualization of the renal vein and artery. We used 3 or 4, 10 or 15 mm Hem-o-Lok clips (Teleflex Medical, Research Triangle Park, NC, USA) to control the renal artery. The renal vein was controlled by 3 or 4, 15 mm clips. We removed the kidney, which was surrounded by the perinephric fat and enveloped by Gerota's fascia, with or without a concomitant adrenalectomy. All of the specimens were removed intact without morcellation or fragmentation in an Endo Catch retrieval bag (Covidien, Dublin, Ireland) through a lower abdominal incision. An indwelling Jackson-Pratt drain was placed in the retroperitoneal space through a 5 mm port site in all of the patients. Para-aortic or paracaval and hilar LND were performed in the same way as ORN.

The continuous variables were compared with an independent Student's t-test. The categorical variables were assessed by using the chi-square test. The 5-year overall survival, the cancer-specific survival, and the recurrence-free survival were analyzed by using the Kaplan-Meier method. All p-values were 2-sided, and $p < 0.05$ was considered significant. Analyses were conducted by using the SPSS ver. 12.0 software (SPSS Inc., Chicago, IL, USA).

RESULTS

There were no significant differences in age, sex, BMI, or tumor laterality between the LRN and ORN groups. The pathologic data, including tumor size and grade, did not differ significantly between the groups (p=0.593 and p=0.857, respectively). The mean operative time was similar in the LRN and ORN groups (209.0 minutes vs. 205.1 minutes, p=0.755). There was a significant increase in ABL in the ORN group (287.6 ml vs. 431.5 ml, p=0.035). The complication rate did not differ statistically between the LRN and ORN groups (6.0% vs. 14.2%, p=0.265). There were no ma-

TABLE 1. Comparison of patients' demographic data and perioperative surgical outcomes between LRN and ORN

	LRN	ORN	p-value
No. of patients	33	35	
Age (yr)	56.1±11.9	55.0±10.8	0.700
Sex (M/F)	24/9	22/13	0.385
BMI (kg/m^2)	24.4±2.6	23.2±3.1	0.104
Tumor laterality (Rt/Lt)	21/12	16/19	0.138
Mean tumor size (cm)	8.2±1.2	9.0±2.0	0.593
Tumor grade (Fuhrman)			0.857
2	14	15	
3	18	18	
4	1	2	
Operation time (min)	209.0±55.3	205.1±48.5	0.755
ABL (ml)	287.6±281.1	431.5±269.6	0.035
Transfusion rate (%)	7/33 (21.2)	6/35 (17.1)	0.314
Complication rate (%)	2/33 (6.0)	5/35 (14.2)	0.265

BMI: body mass index, ABL: actual blood loss ($EBVx(Hgb_i - Hgb_f) / ((Hgb_i + Hgb_f)/2) + (500xT(u))$, Hgb_i: preoperative hemoglobin, Hgb_f: postoperative day one morning hemoglobin, T(u): sum of autologous whole blood (AWB), packed red blood cells (PRBC), and cell saver (CS) units, LRN: laparoscopic radical nephrectomy, ORN: open radical nephrectomy. Data presented as the mean±standard deviation

jor complications that required conversion to an open procedure or reoperation. According to the complication classification system suggested by Clavien et al [15], 2 (100%) complications in the LRN group were grade I; in the ORN group, 4 (80%) were grade I and 1 (20%) was grade II. Grade III or IV complications did not occur in our series. Two cases of chylous ascites occurred in the LRN group; 1 case of pneumothorax and 2 cases of pneumonia and ileus occurred in the ORN group. All cases were managed by conservative treatment (Table 1).

The mean follow-up was 60.0 months (range, 48.0-77.0 months) in the LRN group. Cancer recurrence was noted in 5 patients between 24 and 57 months; in all cases, the lung was the site of recurrence. Two of 5 patients died at 58 and 66 months after nephrectomy, respectively. The other 3 patients displayed recurrences at 24, 35, and 47 months; they survived to 50, 55, and 56 months, respectively. The 5-year overall survival, the cancer-specific sur-

TABLE 2. Comparison of long-term oncologic outcomes between

	LRN	ORN	p-value
Mean follow up (mo)	60.0±10.7	65.6±7.0	
Distant metastases (%)	5	6	0.597
Lung	5 (100.0)	3 (50.0)	
Bone	0 (0.0)	1 (16.7)	
Liver	0 (0.0)	2 (30.3)	
% 5-year survival			
Overall	87.8	85.7	0.513
Cancer-specific	93.9	88.5	0.910
Recurrence-free	84.8	85.7	0.842

LRN: laparoscopic radical nephrectomy, ORN: open radical nephrectomy

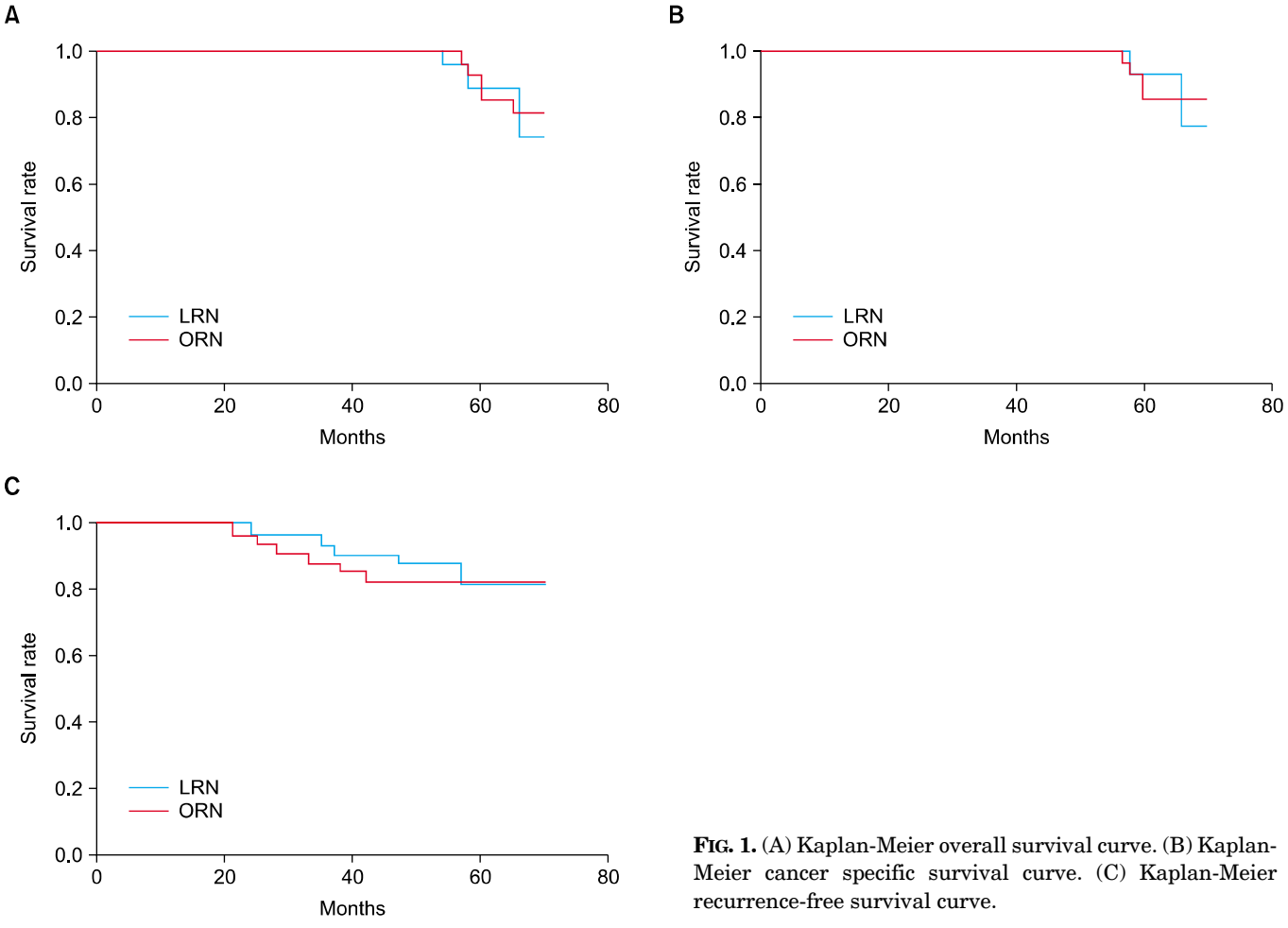

FIG. 1. (A) Kaplan-Meier overall survival curve. (B) Kaplan-Meier cancer specific survival curve. (C) Kaplan-Meier recurrence-free survival curve.

vival, and the recurrence-free survival rates were 87.8%, 93.9%, and 84.8%, respectively (Table 2).

The mean follow-up was 65.6 months (range, 56.0-77.0) in the ORN group. Cancer recurrence was noted in 6 patients between 21 and 42 months; the site of recurrence was the lung in 3 cases, the liver in 2 cases, and the bones in 1 case. Four of 6 patients died between 57 and 60 months. The other 2 patients exhibited recurrence at 28 and 38 months; they lived to 55 months after the operation. The 5-year overall, cancer-specific, and recurrence-free survival rates were 85.7%, 88.5%, and 82.8%, respectively (Table 2).

For the LRN and ORN groups, respectively, the 5-year overall survival rate, the cancer-specific survival rate, and the recurrence-free survival rate were not significantly different. The 5-year overall survival rates were 87.8% and 85.7% (p=0.513), respectively; the cancer-specific survival rates were 93.9% and 88.5% (p=0.910), respectively; and the recurrence-free survival rates were 84.8% and 82.8% (p=0.842), respectively. Kaplan-Meier curves for the 5-year overall survival rate, the cancer-specific survival rate, and the recurrence-free rate are presented in Fig. 1.

DISCUSSION

Recently, the operative and the oncologic efficacy of laparoscopic applications have been established by numerous studies [2-9]. LRN has emerged as the standard of care in most patients with T1 RCC who are not candidates for nephron-sparing surgery [2,3]. However, most studies were confined to small-sized tumors; few recent publications have addressed the role of LRN for large renal tumors. Moreover, recent studies have suggested the use of nephron-sparing techniques for small-sized renal tumors; these techniques include partial nephrectomy, radio-frequency ablation, and cryotherapy. Therefore, the indications for LRN are expanding to encompass increasingly larger tumors [13].

Dunn et al reviewed the Washington University 9-year experience with LRN; all tumors were $\geq$4 cm and $<$10 cm [10]. The operative time was longer in LRN than in ORN (321 minutes vs. 143 minutes, $p<0.001$); however, the estimated blood loss (EBL) was significantly less and hospital stay was significantly shorter. Steinberg et al compared the operative outcomes for LRN and ORN in T2 RCC [16]. LRN was associated with a shorter operative time (180 minutes vs. 207 minutes, p=0.03), reduced EBL, and a shorter hospital stay. Kim et al retrospectively evaluated the results of LRN and ORN groups with respect to T2 RCC [12]. LRN was associated with a shorter operative time (190.9 minutes vs. 213.8 minutes, p=0.039), less EBL, and a shorter hospital stay. Several institutions have reported various LRN operative times for T2 RCC; however, the blood loss and the length of the hospital stay were generally less in LRN than in ORN. In our study, LRN had an operative time (209.0 minutes vs. 205.1 minutes, p=0.755) and complication rate (6% vs. 14%, p=0.265) similar to ORN. However, the LRN group showed significantly less ABL (287.6 ml vs. 431.5 ml, p=0.035) than did the ORN group. Our LRN operative times were somewhat longer than for ORN. We think that the many cases of LRN during the early period of the learning curve influenced the operative times for LRN in our study. More recently, the LRN operative time for T2 RCC is about 150 minutes in our clinic, which seems to be short compared with the operative times for ORN. We believe that LRN for T2 RCC has more benefit than ORN in operative times. Shorter operative times may have a favorable effect on the patient's postoperative period.

The transperitoneal approach has the benefit of a wider working space and readily identifiable anatomical landmarks. Moreover, it may be advantageous in patients with hilar lymphadenopathy and renal vein involvement [10, 17,18]. Larger tumors occupy an increased proportion of the retroperitoneum, often protruding into the abdominal cavity, thus limiting the space available for laparoscopy. Larger tumors are also more vascular, and there is an increased incidence of multiple feeding vessels in larger renal cancers. It is generally accepted that the necessity of LND is greater for larger renal tumors than for small renal tumors. Therefore, LRN is a technical challenge, even when performed by experienced laparoscopic surgeons. We performed all laparoscopic surgeries by using the transperitoneal approach to create a larger working space, to identify the perinephric space, and to perform LND in case it was necessary.

Long-term oncologic outcomes after ORN for T2 RCC are well documented, but LRN cases remain rare. Portis et al analyzed 64 patients undergoing LRN and 69 patients undergoing ORN before 1996 (median follow-up, 54 months) and reported that the 5-year overall, cancer-specific, and recurrence-free survival rates in the LRN groups for patients with RCC $\geq$7 cm were 89%, 100%, and 87%, compared with 86%, 83%, and 87%, respectively, in the ORN groups [19]. Hemal et al reported on 112 patients with pathological T2 RCC treated with LRN and ORN [20]. The 5-year overall, cancer-specific, and recurrence-free survival rates for LRN were 87.8%, 95.1%, and 92.6%, compared with 88.7%, 94.4%, and 90.1%, respectively, for ORN. Berger et al presented long-term oncologic outcomes of 73 LRN patients [21]. The 5-year overall, cancer-specific, and recurrence-free survival rates for LRN in T2 RCC were 81.0%, 90.0%, and 92.0%. In these retrospective reviews, the authors demonstrated that long-term survival after LRN was equivalent to that after ORN. Our primary aim was to report the long-term oncologic outcome of LRN for the management of T2 RCC. Therefore, we compared our results with other laparoscopic series. In the LRN groups, our 5-year overall, cancer-specific, and recurrence-free survival rates were 87.8%, 93.9%, and 84.8%, respectively. These results seem to be similar to the long-term oncologic outcomes reported in other laparoscopic series. In addition, in the ORN groups, our 5-year overall, cancer-specific, and recurrence-free survival rates were 85.7%, 88.5%, and 82.8%, respectively. These results are also consistent with

the LRN groups. As a result, we conclude that LRN is efficacious as a therapeutic modality for large renal cancer and will have an impact on oncologic outcome.

The limitations of our study were that it was retrospective and nonrandomized. However, it is very difficult to perform a prospective randomized study for LRN vs ORN outcomes in T2 RCC. Our study is significant in that the mean follow-up time was long enough to evaluate the long-term oncologic outcomes of LRN and ORN, and the surgical techniques were standardized. Moreover, this is the first report of the long-term oncologic outcomes of LRN for T2 RCC in Korea.

CONCLUSIONS

Large renal tumors ($\geq$7 cm) can be safely resected laparoscopically with less blood loss than is involved in open radical nephrectomy, with comparable surgical outcomes. During long-term follow-up, LRN achieved a degree of cancer control similar to that obtained with ORN. A larger, population-based study appears to be necessary for further validation of these findings.

Conflicts of Interest

The authors have nothing to disclose.

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