

CLINICAL SCIENCES

ONCOLOGICAL OUTCOMES OF LAPAROSCOPIC RADICAL NEPHRECTOMY FOR RENAL CANCER

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PURPOSE: To report the 5-year oncological outcomes of patients undergoing laparoscopic radical nephrectomy for renal cancer compared to a cohort of patients undergoing open radical nephrectomy.

METHODS: We retrospectively analyzed the data of 88 patients undergoing radical nephrectomy for renal cell carcinoma prior to January 2000. Of these, 45 patients underwent laparoscopic radical nephrectomy, and 43 patients underwent open radical nephrectomy. Inclusion criteria comprised clinically organ-confined tumors of 15 cm or less in size without concomitant lymphadenopathy or vena cava thrombus. Oncological follow-up data were obtained from charts, radiological reports, and phone calls to patients or their families, and were calculated from the date of surgery to the date of last appointment with physician or date of death.

RESULTS: All laparoscopic procedures were completed without open conversion. On comparing the laparoscopic radical nephrectomy and open radical nephrectomy groups, mean tumor size was 5.8 vs 6.2 cm ($P = .44$), mean blood loss was 183 vs 461 mL ($P = .004$), and mean operative time was 2.8 vs 3.7 hrs ($P < .001$). Over a mean follow-up of 5 years in the laparoscopic radical nephrectomy group and 6 years in the open radical nephrectomy group, the overall survival was 81% vs 79% ($P = .47$), and cancer-specific survival was 90% vs 92% ($P = .70$), respectively.

CONCLUSIONS: Laparoscopic radical nephrectomy for renal cancer confers equivalent 5-year oncological outcomes to those of open surgery.

KEYWORDS: Cancer. Laparoscopy. Radical nephrectomy. Outcomes. Survival.

INTRODUCTION

The surgical management of renal mass has changed significantly in the last decade. The oncological principles of open radical nephrectomy (ORN) are duplicated with the laparoscopic approach, but with lower morbidity; therefore, the laparoscopic approach is now considered the standard

of care when nephron-sparing surgery cannot be performed.¹ Herein, we present the 5-year oncological outcomes of laparoscopic radical nephrectomy (LRN) compared with a contemporary series of open radical nephrectomy from a single institution.

METHODS

Patients undergoing radical nephrectomy for renal cell carcinoma were retrospectively analyzed with Institutional Review Board approval. The inclusion criteria for this study comprised patients with renal tumor ≤ 15 cm in largest dimension without any radiological evidence of vena cava involvement, local perinephric extension, or lymph node enlargement. Of the patients who fit the selection criteria, com-

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plete data were available for 88 patients. Laparoscopic radical nephrectomy was performed in 45 patients, and ORN was performed in 43 patients. Routine preoperative radiographic imaging included chest x-ray and abdominal CT or MRI scan. For patients undergoing LRN, data were prospectively entered and maintained in our radical nephrectomy registry.

Demographic data is presented in Table 1. In the LRN group, 29 (64%) patients were men, mean age was 59 ± 12 yrs, tumor size was 5.8 ± 2.5 cm, and the right kidney was involved in 25 (55%) patients. In this group, the retroperitoneoscopic approach was employed in 36 (80%) procedures. In the ORN group, 33 (76%) patients are men, and mean age was 60 ± 11 yrs.

Table 1 - Baseline and intraoperative data

	Laparoscopic	Open	P value
n	45	43	-
Male sex (%)	29 (64)	33 (76)	.29
Age (yrs)*	59 ± 12	60 ± 11	.68
Tumor size (cm)*	5.8 ± 2.5	6.2 ± 2.5	.44
Right side (%)	25 (55)	24 (55)	.81
Retroperitoneal approach (%)	36 (80)	-	-
Clinical stage			.17
T1	36 (80%)	29 (67%)	
T2	9 (20%)	14 (33%)	
Blood loss (mL)*	183 ± 230	461 ± 396	.004
Hospital stay (days)*	1.4 ± 0.8	3.9 ± 2.7	< .001

* Mean ± standard deviation

The employed laparoscopic technique for radical nephrectomy has been described previously.¹ Briefly, during the retroperitoneal approach, a working space is created with balloon dilation, and a 3-port technique is utilized. The renal hilum is dissected to isolate and control the renal artery and vein sequentially. The kidney is dissected outside the intact Gerota's fascia. Concomitant adrenalectomy is performed in patients with an upper pole tumor or with radiographic evidence of adrenal involvement. With the transperitoneal approach, a 4-port technique is utilized. The overlying bowel is reflected medially, and the major renal vessels are dissected, individually clipped, and divided. In either approach, the entrapped specimen is extracted intact through a muscle-splitting, low Pfannenstiel incision without morcellation. The open approach for radical nephrectomy was performed according to well-established techniques. In addition, residents and/or fellows-in-training were assisting the staff surgeon in all cases for both approaches.

Follow-up data were obtained from charts, radiographic reports, and direct phone calls to patients or patient's families, and were calculated from date of surgery to date of last appointment with physician or date of death.

The laparoscopic and open radical nephrectomy groups

were compared using *t* test or Wilcoxon rank sum test (for continuous variables) and chi-square or Fisher exact test (for categorical variables). Kaplan-Meier survival analysis was used to estimate the overall and cancer-specific survival. Comparisons were made for these survival estimates among the patients having open surgical and laparoscopic approaches. Cox regression models were used to assess the effect of surgery type after adjusting for age and tumor size.

RESULTS

All 45 LRN were completed without open conversion or perioperative mortality. On comparing LRN and ORN groups, blood loss was 183 ± 230 mL vs 461 ± 396 mL (*P* < .001), mean operative time was 2.8 ± 0.8 hrs vs 3.5 ± 1.5 hrs (*P* < .01), and mean hospital stay was 1.4 days (range, 1-6 days) vs 3.9 days (range, 3-10 days) (*P* < .001), respectively. Concomitant adrenalectomy was performed in 31 cases (70%) in the LRN group vs 28 (65%) in the ORN group (*P* = .51). Postoperative complications occurred in 3 patients (7%): prolonged ileus, wound dehiscence, and deep vein thrombosis in 1 patient each. Final histopathology data regarding tumor type and stage according to the American Joint Committee on Cancer from 2002 are presented in Table 2. Pathological stage was ≤ pT2 in 88% of patients in the LRN group and 86% of patients in the ORN group. Positive surgical margins for cancer were found in 1 patient in the LRN group and none in the ORN group.

Mean follow-up for the LRN group was 60 months (19-91months). On final analysis, 37 patients were alive and 8 had died; 4 from the renal malignancy. Thus, 5-year over-

Table 2 - Histology and pathological stage

	Laparoscopic	Open	P value
Histology			
Clear Cell	37 (82%)	37 (86%)	.96
Papillary	8 (18%)	6 (14%)	
Pathological stage (%)			.21
pT1a	19 (42%)	16 (37%)	
pT1b	18 (40%)	16 (37%)	
pT2	3 (6%)	5 (12%)	
pT3a	2 (5%)	5 (12%)	
pT3b	2 (5%)	1 (2%)	
pT4	1 (2%)	Zero	
Tumor grade (%)			.17
Grade 1	11 (24%)	4 (9%)	
Grade 2	22 (49%)	24 (56%)	
Grade 3	7 (16%)	11 (26%)	
Grade 4	5 (11%)	4 (9%)	
Concomitant adrenalectomy (%)	31 (70%)	28 (65%)	.51
Multifocal tumors (%)	1 (2%)	2 (4%)	
Positive margin	1 (2%)	Zero	

all and cancer-specific survival was 81% and 90%, respectively. At last follow-up, all patients that were alive had no evidence of metastatic disease; and 1 patient (2%) had developed a local recurrence in the renal fossa. This patient had a pT4 stage (tumor was invading the psoas muscle). The patients with metastatic kidney cancer had a mean survival of 25.2 months, while the patients who died from other causes had a mean survival of 31.5 months.

In the ORN group, the mean follow-up was 72 months (15-96 months). At last follow-up, 32 patients were alive, and 11 patients died in this period: 3 from metastatic kidney cancer and 8 from other causes. The 5-year overall and cancer-specific survival was 79% and 92%, respectively. The patients who died from metastatic cancer had an average survival of 17.3 months (11-22 months), and the patients who died from non-cancer causes had a survival of 35.3 months (8-60 months).

Survival data were also evaluated according to clinical stage. For T1 tumors (< 7 cm), on comparing LRN (n = 36) vs ORN (n = 29) groups, the 5-year outcomes were similar regarding cancer-specific survival (97% vs 96%, log rank = 0.89) and overall survival (85% vs 79%, log rank = 0.26). Similarly for pT2 tumors, the cancer-specific survival (66% vs. 85%, log rank = 0.37) and overall survival (66% vs 78%, log rank = 0.64) were also comparable between groups.

Table 3 - Cox regression model to assess the effect of surgery type after adjusting for age and tumor size

Variable	Hazard ratio (95% confidence interval)	P value
Overall		
Laparoscopic surgery	1.613 (0.693, 3.757)	.27
Age	1.712 (1.189, 2.464)	.004
Tumor size	1.115 (0.976, 1.274)	.11
Patients who died from kidney cancer		
Laparoscopic surgery	0.395 (0.047, 3.319)	.39
Age	0.936 (0.240, 3.655)	.92
Tumor size	0.595 (0.353, 1.003)	.05
Patients who died from other cause		
Laparoscopic surgery	0.947 (0.266, 3.372)	.93
Age	1.364 (0.729, 2.552)	0.33
Tumor size	1.130 (0.886, 1.441)	0.33

Table 4 - Laparoscopic radical nephrectomy oncological outcomes

Author	n	Follow-up (yrs)	Conversion	Blood loss (mL)	Operative Time (hr)	Hospital stay (days)	Projected 5-year, disease-free survival
Dunn2000 ³	44	2.1	1	NA	5.5	3.4	91%
Chan2001 ⁴	66	2.9	1	280	4.2	3.8	95%
Ono2001 ⁵	102	2.4	4	254	4.7	N/A	95%
Portis2002 ⁶	64	4.5	N/A	219	N/A	4.8	98%
Saika2003 ⁷	195	3.3	7	248	4.6	N/A	87%
Permpongkosol2005 ⁸	121	6	1	280	4.2	3.8	94%*
Present Study	45	5	0	179	2.8	1.4	92%*

*Actual 5-year survival.

Cox regression models did not show a significant difference between the two techniques, after adjusting for patient's age and tumor size (Table 3).

DISCUSSION

Since the initial report of laparoscopic nephrectomy in 1991 by Clayman,² laparoscopic radical nephrectomy (LRN) has evolved, and in experienced hands has become the gold standard treatment for most of patients with renal cancer. The major advantages of the minimally invasive approach include lower perioperative morbidity, with less blood loss, shorter length of hospital stay, and quicker convalescence.^{1,3} However, long-term oncological data remain scanty in the literature (Table 4).

Dunn et al reported 60 LRNs with 1 open conversion, having a mean operative time of 5.5 hrs, mean blood loss of 170 mL, and overall transfusion rate of 12%.³ Minor and major complications occurred in 34% and 3% of cases, respectively. Short-term oncological results were comparable to ORN, at a mean follow-up of 25 months. Chan et al presented 67 LRNs, with 1 open conversion, estimated mean blood loss of 290 mL, mean operative time of 4.2 hrs, and hospital stay of 3.8 days.⁴ Overall complications occurred in 15% of cases, with a blood transfusion rate of 8%. In that study, the overall survival with a mean follow-up of 35 months was 86%.

In the series of 103 LRNs published by Ono et al with a follow-up of 29 months, the cancer-specific and overall survival was 98% and 93%, respectively.⁵ In a multi-institutional analysis of 64 patients undergoing LRN by Portis et al, the estimated 5-year cancer-specific and overall survival was 98% and 81%, respectively.⁶

Saika et al reported 188 LRNs, with an estimated 5-year cancer-specific and overall survival of 94% and 87%, respectively.⁷ In that series, 7 open conversions were noted, with a mean operative time of 4.6 hrs, mean blood loss of 250 mL, and perioperative complication rate of 15%.

In the recently published study of Permpongkosol et al. with a median follow-up of 73 months, the actuarial can-

cer-specific and overall survival at 10 years was of 97% and 76%, respectively, which was similar to that of the ORN.⁸

In each of the above series, the oncological outcomes of LRN were similar to ORN as evaluated by calculated 5-year cancer-specific and overall survival.

Focusing on clinical T2 tumors at our institution, Steinberg et al compared 65 LRNs (tumor size of 9.2 cm) with ORNs (tumor size of 9.9 cm), with superior perioperative outcomes for blood loss, operative time, hospital stay, and convalescence for the LRN group.⁹

The 5-year cancer-specific survival results for T1 and T2 tumors were also not statistically different between the groups in the present study, presenting similar results with the those of the ORN series reported by Tsui et al,¹⁰ and with the series published by Frank et al from Mayo Clinic with 2746 patients.¹¹ In addition, we did not have any contralateral recurrence, a fact that may be secondary to absence of positive margins and low incidence of multifocal tumors. As reported by Bani-Hani et al,¹² these two factors are risk factors for contralateral recurrence for clear-cell renal cell carcinoma while nuclear grade was a significant predictor of contralateral recurrence for papillary renal cell carcinoma.

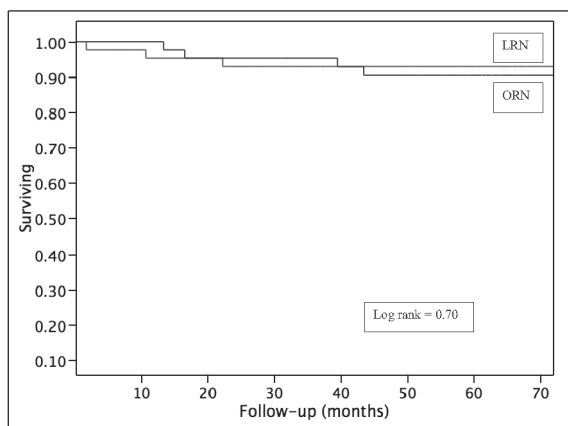


Figure 1 - Cancer-specific survival; laparoscopic radical nephrectomy (LRN) vs open radical nephrectomy (ORN).

The retroperitoneal approach is preferentially used at our institution unless relative contraindications exist, such as larger tumors (>10 cm) or prior retroperitoneal surgery. Nambirajan et al¹³ in the first prospective, randomized controlled study found no difference between the two approaches, when the procedure was performed by an experienced laparoscopic surgeon. More recently, Desai and al¹⁴ showed no difference in the results comparing the two ap-

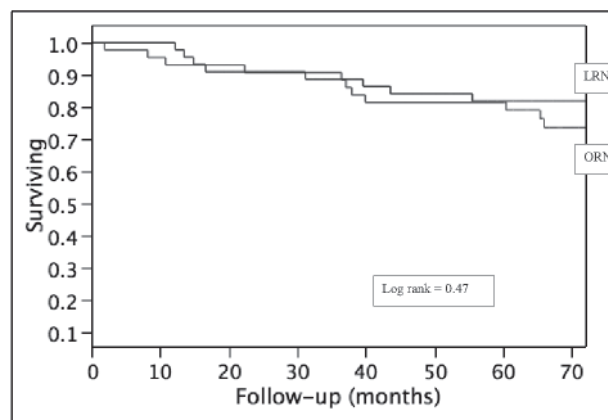


Figure 2 - Overall survival; laparoscopic radical nephrectomy (LRN) vs open radical nephrectomy (ORN).

proaches in the context of a prospective, randomized study. The specimen extraction was performed without morcellation in all cases.

We believe that relevant information from pathological analysis would be lost with morcellation, and the aesthetic advantages do not justify the morcellation, although a prospective, randomized trial has not yet been published comparing the oncological outcomes between these techniques.¹⁵

From the financial standpoint, after the initial learning curve, LRN is 12% less expensive than ORN at the authors' institution.¹⁶

The weaknesses of this study are inherent in its retrospective design, as such selection bias and lack of control. The strengths include long and reliable follow-up, and data collection for similar periods of time, minimizing the differences in renal cancer care over time. We used tumor size and age in the statistical model to control for any clinical difference between groups.

Indications for LRN are expanding in excellence centers worldwide, using the minimally invasive approach for larger tumors, patients with previous abdominal surgery, level I renal vein involvement, and cytoreductive nephrectomy.^{17,18} We believe that the data presented support the role of LRN as the standard treatment for renal cancer when nephron-sparing surgery is not suitable.

CONCLUSION

Our data show that laparoscopic radical nephrectomy has a low complication rate and 5-year oncological outcomes comparable to open radical nephrectomy for T1 and T2 renal cancer.

RESUMO

Colombo JR Jr, Haber GP, Aron M, Cocuzza M, Colombo R, Kaouk J, Gill IS. Resultados oncológicos da nefrectomia radical laparoscópica no tratamento do carcinoma renal. Clinics. 2007;62(3):251-6.

OBJETIVO: Relatar os resultados oncológicos após 5 anos de seguimento em pacientes submetidos a nefrectomia radical laparoscópica para tratamento do câncer renal, comparando esses com os resultados obtidos com um grupo de pacientes submetidos a nefrectomia radical aberta.

MÉTODOS: Foram analisadas retrospectivamente as informações obtidas de 88 pacientes submetidos a nefrectomia radical para o tratamento do carcinoma renal realizadas previamente a Janeiro de 2000. Destes pacientes, 45 foram tratados com nefrectomia radical laparoscópica e 43 com nefrectomia radical aberta. Foram incluídos pacientes com tumores localizados com tamanho máximo de 15 cm, sem adenopatia ou sinal de envolvimento de veia renal na avaliação radiológica pré-operatória. As informações sobre o seguimento dos pacientes foram obtidas a partir de prontuários, laudos de exames radiológicos e ligações telefônicas para pacientes e/ou

familiares. O seguimento foi calculado desde a data da cirurgia até a última consulta médica ou data de falecimento.

RESULTADOS: Todos os procedimentos laparoscópicos foram realizados sem conversão para a técnica aberta. O tamanho médio tumoral foi de 5.8 e 6.2 cm ($P=0.44$), perda sanguínea estimada de 183 e 461 mL ($P=0.004$), e tempo operatório de 2.8 e 3.7 horas ($P<0.001$), respectivamente para os grupos nefrectomia radical laparoscópica e nefrectomia radical aberta. O tempo de seguimento médio foi de 5 anos para o grupo nefrectomia radical laparoscópica e 6 anos para o grupo nefrectomia radical aberta. A sobrevida global após 5 anos foi de 81% e 79% ($P=0.47$), e a sobrevida específica para cancer foi de 90% e 92% ($P=0.70$), para os grupos nefrectomia radical laparoscópica e nefrectomia radical aberta respectivamente.

CONCLUSÃO: A nefrectomia radical laparoscópica tem resultados oncológicos em 5 anos similares a técnica convencional aberta.

UNITERMOS: Câncer renal, Laparoscopia, Nefrectomia radical, Resultados, Sobrevida

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