Comparison of Partial and Radical Laparascopic Nephrectomy: Long-Term Outcomes for Clinical T1b Renal Cell Carcinoma

Yi Cai, Han-Zhong Li, Yu-Shi Zhang*

Purpose: To compare the long-term clinical and oncologic outcomes in patients treated with laparoscopic partial nephrectomy (LPN) and laparoscopic radial nephrectomy (LRN) for clinical T1b renal cell carcinoma.

Materials and Methods: We retrospectively reviewed the records of all patients who underwent LPN or LRN for a single clinical T1b tumor between January 2005 and January 2012, an actual follow-up of 2-year or greater was available in 39 and 160 after LPN and LRN, respectively. Survival was calculated using the Kaplan-Meier method. Multivariable Cox regression analysis was done to assess predictors of survival.

Results: The two cohorts of patients were similar in age, sex, body-mass index and preoperative eGFR. There were no differences in tumors size (4.97 vs 5.29cm, $P = .08$), and pathological stage distribution between the two cohorts. The median follow-up after LPN and LRN were 67 (range: 18-118) and 70 (19-120) months, respectively. For LPN versus LRN, 5-years overall and cancer specific survival rates were 93.33% vs 85.69% and 96.00% vs 91.35%, respectively. For LPN versus LRN, 10-years overall and cancer specific survival rates were 85.56% vs 73.41% and 88.00% vs 82.85%, respectively. On multivariate analysis, patients' age, ASA score and pathological stage were the major factors affecting overall survival, and patients' age and pathological stage were associated with cancer specific survival. The percent decrease in glomerular filtration rate was significantly lower in the LRN group at early and last followup.

Conclusion: LPN is an effective treatment option in appropriately selected patients with cT1b RCC. It provides 5-year, 10-year overall survival and cancer specific survival comparable to those of LRN as well as better preservation of renal function than LRN. Overall survival and cancer specific survival are associated with nonmodifiable factors but not by the choice of operative technique.

Keywords: renal cell carcinoma; T1b; laparoscopy; partial nephrectomy.

INTRODUCTION

Partial nephrectomy (PN) is the current standard of care for localized RCC, especially in patients with tumors < 4cm[1,2]. The oncological equivalence and better functional outcomes of PN compared to radical nephrectomy (RN) for T1a renal cell carcinoma have been widely reported. Further, PN is associated with improved quality of life, preservation of renal function and potentially improved overall survival. However, up to 25% of RCCs are still detected at a size of 4 ~7cm (T1b), for which RN was the gold standard of treatment in the last decades[3]. Recent data suggest that PN should be performed if feasible for T1b renal tumors[4,5]. With advances in laparoscopic suturing techniques and the availability of hemosealant substances, laparoscopic partial nephrectomy (LPN) has also become a well-defined method[6,7]. In fact, LPN for T1b renal tumor has been demonstrated to be feasible in expert hands[8,9]. There are some studies about the short-term oncological and renal function outcome of LRN or LPN on T1b renal tumors[7]. However, the long-term clinical and oncologic outcomes of LRN and LPN remain to be defined.

In the current study, we reviewed a single-institution database of patients treated with LPN and LRN for clinical T1b renal cell carcinoma to assess long-term clinical and oncologic outcomes.

MATERIALS AND METHODS

Study design

Institutional review board approval was obtained for this retrospective study. We reviewed the records of all patients who underwent LPN or LRN between January 2005 and January 2012 at Peking Union Medical College Hospital. All patients were preoperatively evaluated with computed tomography or magnetic resonance imaging. Only those with histologically confirmed RCC, a solitary tumor with a maximum diameter of 4.0 to 7.0 cm (clinical stage T1b) and a minimum 2-year post treatment radiographic follow up were included in analysis. Patients with synchronous bilateral, clinic stage tumor (cT) ≥ 2, benign tumors in pathology specimens and those who underwent open surgery (laparoscopic switch open surgery also was excluded) were excluded from study. In addition, patients with solitary kidneys or end-stage renal disease (ESRD) (stage 5, estimated glo-

Department of Urology, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College. 1 Shuaifuyuan Road, Beijing, China, 100730.
*Correspondence: Department of Urology, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing 100730, China.
Tel: +86 138 1003 3903. Fax: +86 010-8915 2510. E-mail: zhangyushi2014@126.com.
Received March 2017 & Accepted

Table 1. Baseline demographics and patient characteristics.

Characteristics	LPN(n=39)	LRN(n=160)	*p*-Value
Age, median(range)	53 (38-74)	54 (20-79)	0.632
Gender (%)			
Male(%)	26 (67%)	97(61%)	0.486
Female(%)	13 (33%)	63(39%)	
BMI(kg/m^2), mean±SD	23.55 ± 3.82	23.25 ± 4.19	0.654
ASA score, mean±SD	1.96 ± 0.44	1.95 ± 0.49	0.461
Follow-up(months), median(range)	67 (18-118)	70 (19-120)	0.293
Laterality			
Right(%)	21 (54%)	68 (43%)	0.201
Left(%)	18 (46%)	92 (57%)	
No. hypertension (%)	13 (33%)	55 (34%)	0.902
No. diabetes mellitus (%)	4 (10%)	24 (15%)	0.445
No. coronary artery disease (%)	1 (3%)	6 (4%)	0.718
Mean tumor size (cm), mean±SD	4.97 ± 0.75	5.29 ± 0.74	0.082
No. histology (%):			
Clear cell RCC	28 (72%)	129 (81%)	0.226
Other RCC subtype	11 (28%)	31 (19%)	
papillary RCC	8	15	
chromophobe RCC	3	12	
Translocation RCC Xp11.2	-	2	
carcinoma of the collecting ducts of Bellini	-	2	
Histology feature Sarcomatoid-change (%)	1 (3%)	5 (3%)	0.854
Tumor necrosis (%) 3 (8%)	15 (9%)	0.743	
No. Fuhrman nuclear grade (%)			
1 or 2	30 (77%)	115 (72%)	0.525
3 or 4	9 (23%)	45 (28%)	
PSM	1(3%)	-	
pT stage, (%)			
pT1	37 (95%)	145 (91%)	0.394
≥ pT2	2 (5%)	15 (9%)	
GFR ml/min/1.73m^2			
Pretreatment	78.94 ± 18.74	85.27 ± 19.87	0.091
Early	66.43 ± 23.08	59.59 ± 15.42	0.042
Latest	67.14 ± 17.07	52.36 ± 13.21	< 0.001
Median % renal functional decrease	15.04%	38.59%	< 0.001

Abbreviations: BMI,body-mass index; LPN,laparoscopic partial nephrectomy; LRN,laparoscopic radical nephrectomy; ASA, American Society of Anesthesiologists; PSM, positive surgical margins; pT stage, pathological tumor stage.

merular filtration rate (eGFR) <15mL/minute/1.73m^2) were excluded from the study as well. Estimated GFR was calculated using the Modification of Diet in Renal Disease equation, eGFR in ml/minute/1.73m2 =186.3×(serum creatinine)-1.154×(age)-0.203 × (0.742 if female)[10].

Statistical analysis

The SPSS software package (version 17.0) was used for all statistical analysis. Between-group comparisons were assessed using Student's t-test, chi-square test, Mann-Whitney test or Fisher exact test. The Kaplan-Meier method was applied to generate survival curves, which were compared using the log rank test. Multivariable Cox regression analysis performed to determine predictors of survival. *P* value < 0.05 was defined as statistically significant.

RESULTS

Patient clinical characteristics

Between January 2005 and January 2012, a total of the 633 patients underwent LPN or LRN, including 39 and 160 patients treated with LPN and LRN, respectively (**Figure 1**). **Table 1** lists patient demographics and tumor characteristics. The mean age in the LPN cohort was 54 (range: 20-79) years and in the LRN cohort was 53 (range: 38-74) years (*P* = .63). There were no differences in tumors size (4.97 vs 5.29cm, *P* = .08), and pathological stage distribution between the two cohorts. The mean follow-up was 67 (range: 18-118) months in the LPN cohort and 70[(19-120)] months in the LRN cohort (*P* = .29). No significant differences were observed between the two groups for patients' sex, body mass index, diabetes mellitus, coronary artery disease, hypertension and preoperative eGFR. There was no significant difference in tumor characteristics between the two cohorts, including the laterality of the affected kidney, histology subtype, Fuhrman nuclear grade, pathologic stage and histology feature (**Table 1**). Only one patient in the LPN cohort was diagnosed with positive surgical margin, because the tumor was located completely within the renal parenchyma. The patient died from cardiovascular disease 36 months after LPN for a 5.2cm clear renal cell carcinoma, however, the patient did not experience local recurrence or metastasis.

Renal function analysis

Table 1 displays renal functional outcomes. Preoperative GFR was 78.94 ± 18.74 and 85.27 ± 19.87ml/minute/1.73m^2 in the LPN and LRN cohorts (*P* = .09), and the early GFR (lowest measured value 7 to 180 days postoperatively) was 66.43 ± 23.08 and 59.59 ± 15.42 ml/minute/1.73m2, respectively (*P* = .04). The latest GFR (value at last followup) was 67.14 ± 17.07 and 52.36 ± 13.21ml/minute/1.73m^2, respectively (*P* < .001). The median percent decrease in GFR was 15.04% and 38.59% after LPN and LRN, respectively (*P* < .001). Renal functional outcomes of LPN were superior to those of LRN both in early and long term follow-up period.

Table 2. Predictors of overall survival and cancer specific survival for patients.

Variables	OS				CSS			
	Univariable HR(95% CI)	P-value	Multivariable HR(95% CI)	P-value	Univariable HR(95% CI)	P-value	Multivariable HR(95% CI)	P-value
Age	1.45 (1.36-1.54)	< 0.001	1.17 (1.10-1.24)	< 0.001	1.07 (1.01-1.12)	0.012	1.16 (1.08-1.23)	0.022
ASA score	1.58 (1.39-1.78)	< 0.001	1.64 (1.21-2.14)	0.008	1.79 (1.12-2.58)	0.043	1.56 (0.97-2.23)	0.094
pT stage (pT1 vs ≥ pT2)	1.98(1.83-2.17)	<0.001	1.39(1.13-1.45)	< 0.001	2.13(1.83-2.79)	< 0.001	1.62(1.23-2.08)	< 0.001
Fuhrman grade (1/2 vs 3/4)	0.47(0.38-0.62)	0.022	0.65(0.19-2.15)	0.482	0.39 (0.22-0.58)	0.031	0.63(0.19-2.12)	0.462
LPN vs LRN	1.45□0.78-3.26□	0.461	1.37(0.41-4.55)	0.603	1.21(0.56-3.78)	0.553	1.13(0.36-3.47)	0.833

Abbreviations: OS, overall survival; CSS, cancer specific survival; pT stage, pathological tumor stage; ASA, American Society of Anesthesiologists; LPN, laparoscopic partial nephrectomy; LRN, laparoscopic radical nephrectomy.

Overall and cancer specific survival analysis

The 5-year and 10-year overall survival (OS) in patients who underwent LPN was 93.33% and 85.56%, respectively, and in the LRN cohort, 85.69% and 73.41%, respectively (log-rank test P = .15) (**Figure. 2A**). The 5-year and 10-year OS seems to be better in the LPN cohort compared with LRN, however, this difference showed marginally significant. In the LPN cohort, the 5-year cancer specific survival (CSS) was 96.00% and 10-year CSS was 88.00%. In the LRN cohort, the 5-year CSS was 91.35% and 10-year CSS was 82.85%. The difference was not significant between the two groups for 5 or 10 year CSS (log-rank test P = .39) (**Figure 2B**). The factors that significantly affected OS were the patients' age, pT stage and preoperative ASA score. Each year of age increased the risk of death by 1.02-fold. The increase of the ASA class one point increased 1.65-fold the risk of death. The increase of the pT stage (pT1 vs. pT2 vs. ≥ pT3) by one unit increased the risk of death by 1.36-fold. OS was not affected by the surgical technique or Fuhrman grade (**Table 2**). CSS was significantly affected by the patients' age and pT stage. However, CSS was not affected by the surgical technique, preoperative ASA score or Fuhrman grade (**Table 2**).

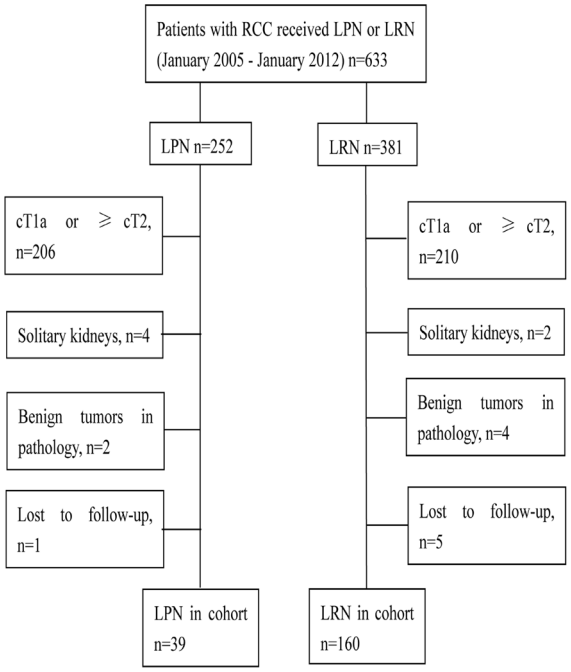

Figure 1. Study population included in analysis.

DISCUSSION

The optimal treatment for clinical T1b RCC is controversial at present, partial nephrectomy is becoming an alternate standard to radical nephrectomy in the management of T1b tumors. Milonas D et al[11] in their study reported that open partial nephrectomy showed better 12-year OS (55.2% vs 53.7%) and CSS (80.6% vs 69.6%) compared with open radical nephrectomy, although no significant differences were observed between the two groups. Emerging data demonstrate feasibility of LPN for increasing the proportion of cT1b tumors; however, recent trends analyses demonstrate that the majority of T1b PN are still carried out by open surgery, and concerns continue about prolonged ischemic times and risk of bleeding[12]. LPN appears to have comparable short-term functional and oncologic outcomes relative to LRN. In one of the most recent studies with about 20 months follow-up conducted by Deklaj T.[8], LPN was an approach to NSS that was feasible and associated with preservation of intermediate-term renal function compared with LRN. A prospective, randomized EORTC intergroup phase 3 study comparing the oncologic outcome of elective nephron-sparing surgery and radical nephrectomy showed that NSS seems to be significantly less effective than RN in terms of OS, however, the major parts of patients were low-stage renal cell carcinoma (≤ 5 cm)[13]. Long-term results of oncologic and functional outcomes comparison of LPN and LRN for clinical T1b renal cell carcinoma remain to be defined. Our study is specific because it reported 10-year oncologic and renal functional outcomes of LPN and LRN for cT1b RCC.

In our study, the 5-year OS in the LRN group was 93.33% compared with 85.69% in the LRN group; and the 10-year OS was 85.56% and 73.41%, respectively. CSS at 5 years was 91.35% and 96.00% in the LRN and LPN groups, respectively; and at 10 years, 82.85% and 88.00%. Better 10-year OS and CSS in LPN cohort were also observed in the current study, although the difference was not significant. On multivariate analysis, patients' age, ASA score and pathological stage were the major factors affecting overall survival, and patients' age and pathological stage was the associated with cancer specific survival. No significant differences in OS or CSS were observed according to surgical approach. There were no local recurrences in LRN group. One patient in the LPN group demonstrated local recurrence and received radical surgery three years after LPN. Then, he got sorafenib treatment and was alive in a recent follow-up. Another one LPN patient was

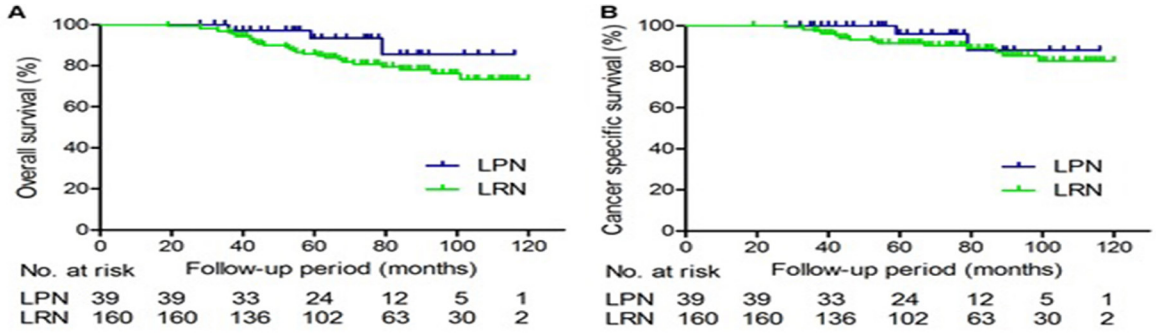

Figure 2. Overall survival **(A)** and Cancer-specific survival **(B)** according the surgical type (LPN vs LRN).

found PSM because the tumor was located completely within the renal parenchyma, although we used scissors to remove the tumor with a margin of 0.5cm. The patient died for cardiovascular disease 3 years after LPN, however, the patient did not experience local recurrence or metastasis. Interesting, several studies demonstrated that PSM were not associated with tumor recurrence, which may be explained by ischemic damage to residual tumor from hemostatic sutures, or intraoperative fulguration of the tumor bed[14,15].

The most important aims of PN is to preserve renal function. In this study, renal functional outcomes of LPN were superior to those of LRN both in early and long term follow-up period. Chronic renal insufficiency is a well-established risk factor for the development of anemia, hypertension, malnutrition, and neuropathy [16,17]. It is associated with poorer quality of life, increased risk of hospitalization, cardiovascular events, and death[18,19]. Better health-related quality of life also represents an advantage of LPN relative to LRN and may cancel out some of the short-term disadvantages of LPN, relative to LRN.

Our study has several limitations[1]. This was a retrospective design with obvious selection bias. However, the baseline patients' characteristics were comparable in the two groups (**Table 1**)[2]. Given the significant number of patients who were lost to followup, survival outcomes in our study may be underestimated or overestimated[3]. Our sample sizes were relatively small. Despite these limitations our results support the clinical usefulness of LPN in approximately selected patients with cT1b RCC. A randomized, controlled trial in larger samples could be ideal and may be done in the future to validate our preliminary results.

CONCLUSIONS

LPN is an effective treatment option in appropriately selected patients with cT1b RCC. It provides 5-year, and 10-year overall survival and cancer specific survival comparable to those of LRN as well as better preservation of renal function than LRN. Overall survival and cancer specific survival are associated with non-modifiable factors but not by the choice of operative technique.

ACKNOWLEDGMENTS

This research was supported by the National Natural Science Foundation of China (81670611) and PUMCH Youth Scientific Research Fund (IH1028800).

CONFLICT OF INTEREST

The other authors declare that they have no competing interests.

REFERENCES

1. Ljungberg B, Bensalah K, Canfield S, et al. EAU Guidelines on Renal Cell Carcinoma: 2014 Update. Eur Urol. 2015;67:913-24.
2. Liss MA, Wang S, Palazzi K, et al. Evaluation of national trends in the utilization of partial nephrectomy in relation to the publication of the American Urologic Association guidelines for the management of clinical T1 renal masses. BMC Urol. 2014;14:101.
3. Karakiewicz PI, Lewinshtein DJ, Chun FK, et al. Tumor size improves the accuracy of TNM predictions in patients with renal cancer. Eur Urol. 2006;50:521-8; discussion 9.
4. Volpe A, Amparore D, Mottrie A. Treatment outcomes of partial nephrectomy for T1b tumours. Curr Opin Urol. 2013;23:403-10.
5. M Crépel CJ, P Perrotte , U Capitanio , H Isbarn , SF Shariat , D Liberman , M Sun , G Lughezzani , P Arjane , H Widmer , M Graefen , F Montorsi , J Patard , PI Karakiewicz Nephron-sparing Surgery Is Equally Effective to Radical Nephrectomy for T1BN0M0 Renal Cell Carcinoma: A Population-based Assessment. Urology. 2010;75:271-5.
6. Simmons MN, Chung BI, Gill IS. Perioperative efficacy of laparoscopic partial nephrectomy for tumors larger than 4 cm. Eur Urol. 2009;55:199-207.
7. Aron M, Gill IS. Minimally invasive nephron-sparing surgery (MINSS) for renal tumours part I: laparoscopic partial nephrectomy. Eur Urol. 2007;51:337-46; discussion 46-7.
8. Deklaj T, Lifshitz DA, Shikanov SA, Katz MH, Zorn KC, Shalhav AL. Laparoscopic radical versus laparoscopic partial nephrectomy for clinical T1bN0M0 renal tumors: comparison of perioperative, pathological, and functional outcomes. J Endourol. 2010;24:1603-7.
9. Alyami FA, Rendon RA. Laparoscopic partial nephrectomy for >4 cm renal masses. Can Urol Assoc J. 2013;7:E281-6.

10. Levey AS, Bosch JP, Lewis JB, Greene T, Rogers N, Roth D. A more accurate method to estimate glomerular filtration rate from serum creatinine: a new prediction equation. Modification of Diet in Renal Disease Study Group. Ann Intern Med. 1999;130:461-70.
11. Milonas D, Skulcius G, Baltrimavicius R, et al. Comparison of long-term results after nephron-sparing surgery and radical nephrectomy in treating 4- to 7-cm renal cell carcinoma. Medicina (Kaunas). 2013;49:223-8.
12. Lee HJ, Liss MA, Derweesh IH. Outcomes of partial nephrectomy for clinical T1b and T2 renal tumors. Curr Opin Urol. 2014;24:448-52.
13. Van Poppel H, Da Pozzo L, Albrecht W, et al. A prospective, randomised EORTC intergroup phase 3 study comparing the oncologic outcome of elective nephron-sparing surgery and radical nephrectomy for low-stage renal cell carcinoma. Eur Urol. 2011;59:543-52.
14. Ani I, Finelli A, Alibhai SM, Timilshina N, Fleshner N, Abouassaly R. Prevalence and impact on survival of positive surgical margins in partial nephrectomy for renal cell carcinoma: a population-based study. BJU Int. 2013;111:E300-5.
15. Favaretto RL, Sanchez-Salas R, Benoist N, et al. Oncologic outcomes after laparoscopic partial nephrectomy: mid-term results. J Endourol. 2013;27:52-7.
16. Go AS, Chertow GM, Fan D, McCulloch CE, Hsu CY. Chronic kidney disease and the risks of death, cardiovascular events, and hospitalization. N Engl J Med. 2004;351:1296-305.
17. Huang WC, Levey AS, Serio AM, et al. Chronic kidney disease after nephrectomy in patients with renal cortical tumours: a retrospective cohort study. Lancet Oncol. 2006;7:735-40.
18. Mukkamala A, He C, Weizer AZ, et al. Long-term renal functional outcomes of minimally invasive partial nephrectomy for renal cell carcinoma. Urol Oncol. 2014;32:1247-51.
19. RH Thompson SB, CM Lohse , BC Leibovich , ED Kwon , JC Cheville , ML Blute Radical Nephrectomy for pT1a Renal Masses May be Associated With Decreased Overall Survival Compared With Partial Nephrectomy. The J Urol. 2008;179:468-73.