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Comparison of Partial and Radical Nephrectomy for pT1b Renal Cell Carcinoma

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Purpose: Partial nephrectomy (PN) for patients with T1a renal cell carcinoma (RCC) has increasingly become accepted, although its role for patients with T1b RCC remains controversial. We retrospectively evaluated and then compared the oncologic and functional outcomes of patients with pT1b RCC who were treated with PN or radical nephrectomy (RN).

Materials and Methods: A total of 70 patients who were diagnosed with pT1bN0M0 RCC between January 1995 and December 2004 were included. The 5-year overall survival (OS), the 5-year recurrence-free survival (RFS), and the 5-year cancer-specific survival (CSS) were compared between the groups. Preoperative and postoperative serum creatinine and estimated glomerular filtration rate (GFR) levels were analyzed to assess renal function.

Results: The 5-year OS (92.3% vs. 87.8%, p=0.501), RFS (92.3% vs. 77.8%, p=0.175), and CSS (92.3% vs. 94.5%, p=0.936) of the PN and RN groups were not statistically different. The proportion of patients with decreased renal function was lower in the PN group than in the RN group (PN=0% vs. RN=11.5%). The postoperative change in serum creatinine and the GFR 1 year after nephrectomy was higher in the RN group than in the PN group (PN=0.2±0.2, 12.1±9.1 vs. RN=0.3±0.5, 18.1±12.5), but there was no statistical difference.

Conclusions: There were no statistically significant differences in prognosis or renal function between patients treated with PN and those treated with RN for pT1b RCC. PN may be a useful treatment modality for patients with pT1b RCC.

Key Words: *Nephrectomy; Prognosis; Renal cell carcinoma*

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INTRODUCTION

The main treatment for renal cell carcinoma (RCC) is radical nephrectomy (RN), and RN has been the gold standard treatment for RCC during the last 2 decades [1]. However, the risk of deteriorated renal function after RN has now been well documented [2]. The incidental detection of renal masses has dramatically increased the number of patients presenting with locally confined RCC, and this calls for multiple options for the surgical therapy [3]. Consequently, there has been a continuous development of partial nephrectomy (PN) to avoid unnecessary destruction of nephrons [3,4].

The benefits of PN include a decreased risk of long-term renal insufficiency and a positive impact on the quality of life [5-7]. Thus, according to the current guidelines, PN is now indicated for RCC less than 4 cm [1]. Although earlier studies suggested that 4 cm be established as the maximum size for PN [1], recent data suggest that it might be possible to extend the success and benefits of PN to treating tumors >4 cm in size [3,8].

Thus, we retrospectively evaluated and compared the oncologic and functional outcomes of patients treated with PN and RN for pT1b stage RCC.

MATERIALS AND METHODS

1. Patients

A total of 70 patients who were diagnosed with pT1bN0M0

RCC between January 1995 and December 2004 were included in this study. All of the patients underwent PN (n=18, 25.7%) or RN (n=52, 74.3%) by an experienced surgeon, and standard techniques were used for both PN (under the cold ischemic condition) and RN. All of the patients underwent surgery with an open method. The preoperative clinical tumor staging workup included computed tomography (CT) or magnetic resonance imaging (MRI) of the abdomen and pelvis and chest radiography.

2. Preoperative and postoperative evaluations

The patients' age, gender, past medical history (diabetes mellitus, hypertension), Charlson comorbidity index score, follow-up duration, body mass index (BMI), preoperative symptoms, and pathologic factors (tumor size, location, histologic type, and Fuhrman's nuclear grade) were investigated. To identify the oncologic outcome, the 5-year overall survival (OS), 5-year recurrence-free survival (RFS), and 5-year cancer-specific survival (CSS) were compared between each group. To evaluate renal function, the preoperative and postoperative (immediate and 1 year after nephrectomy) serum creatinine level and estimated glomerular filtration rate (GFR) were analyzed. The estimated GFR was calculated by using the Modification of Diet in Renal Disease (MDRD) equation.

3. Follow-up evaluations

All the patients received a follow-up visit at 1 to 2 weeks after discharge for assessing their general health status. After the first visit, the patients received follow-up evaluations every 3 or 6 months until the first year, and then annually. At these times, they were evaluated for newly developed symptoms and they underwent careful physical examinations, laboratory tests, and radiologic tests (chest X-ray, ultrasonography [USG], CT). The USG, CT, and/or MRI were checked to evaluate for local recurrence or distant metastasis.

4. Definition

The stage was reassessed according to the 2002 TNM classification system [9]. Decreased renal function was evaluated according to the National Kidney Foundation

TABLE 1. Characteristics of the patients with pT1b renal cell carcinoma

	PN (n=18)	RN (n=52)	p-value
Age (years)	47.3±9.8	57.3±10.7	0.001[a]
Sex			0.811[b]
Male (%)	13 (72.2)	36 (69.2)	
Female (%)	5 (27.8)	16 (30.8)	
Diabetes mellitus (%)	3 (16.7)	5 (9.6)	0.415[b]
Hypertension (%)	2 (11.1)	10 (19.2)	0.718[b]
Charlson comorbidity index score			0.883[b]
0 (%)	10 (55.5)	26 (50.0)	
1 (%)	4 (22.2)	17 (32.7)	
2 (%)	3 (16.7)	6 (11.5)	
≥3 (%)	1 (5.6)	3 (5.8)	
Follow-up duration (months)	78.2±44.1	66.5±43.6	0.310[a]
Body mass index (kg/m^2)	23.1±2.6	23.8±2.8	0.341[a]
Preoperative symptoms (%)	7 (38.9)	21 (40.4)	0.974[b]
Flank pain (%)	6 (33.3)	11 (21.2)	
Gross hematuria (%)	0 (0)	9 (17.3)	
Palpable mass (%)	1 (5.6)	1 (1.9)	
Tumor size (cm)	5.0±0.9	5.5±0.9	0.036[a]
4<size≤5 (%)	11 (61.1)	21 (40.4)	
5<size≤6 (%)	5 (27.8)	19 (36.5)	0.348[b]
6<size≤7 (%)	2 (11.1)	12 (23.1)	
Tumor location			0.473[b]
Upper pole (%)	6 (33.3)	22 (42.3)	
Mid pole (%)	3 (16.7)	13 (25.0)	
Lower pole (%)	9 (50.0)	17 (32.7)	
Histologic type			0.598[b]
Clear cell (%)	13 (72.2)	43 (82.7)	
Papillary (%)	3 (16.7)	6 (11.5)	
Others (%)	2 (11.1)	3 (5.8)	
Fuhrman's nuclear grade			0.417[b]
Grade 1+2 (%)	11 (61.1)	25 (48.1)	
Grade 3+4 (%)	7 (38.9)	27 (51.9)	

PN: partial nephrectomy, RN: radical nephrectomy, [a]: Mann-Whitney U test, [b]: Fisher's exact test

Dialysis Outcomes Quality Initiative Clinical Practice Guidelines [10]. The endpoints consisted of OS, RFS, and CSS. Cancer-specific mortality was defined as death primarily caused by metastatic RCC. Recurrence was defined as radiologically identified metastasis or local recurrence during the study period.

5. Analysis

The 5-year OS, RFS, and CSS were estimated by using the Kaplan-Meier method. The effect of surgery on renal function, according to the serum creatinine levels and estimated GFR, was analyzed by using the Mann-Whitney U test. A 5% level of significance was used for all statistical testing, and all statistical tests were two-sided. The analysis was performed by using the statistical software SPSS (17.0KO for Windows, release 14.0.2).

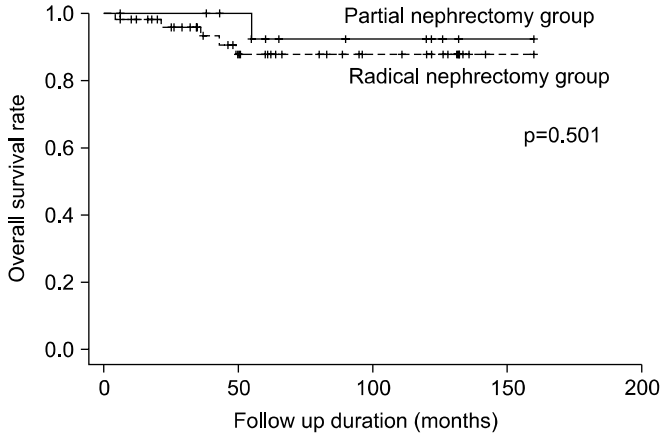

FIG. 1. Kaplan-Meier survival curve estimates of the 5-year overall survival for all patients according to whether they underwent partial nephrectomy or radical nephrectomy.

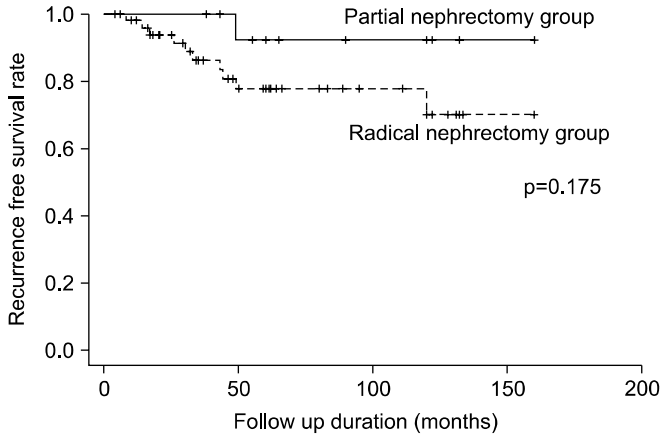

FIG. 2. Kaplan-Meier survival curve estimates of the 5-year recurrence-free survival for all patients according to whether they underwent partial nephrectomy or radical nephrectomy.

RESULTS

The mean ages of the patients were 47.3±9.8 years and 57.3±10.7 years for the PN and RN groups, respectively. The mean follow-up durations of the patients treated with PN and RN were 78.2±44.1 months and 66.5±43.6 months, respectively. The characteristics of the 70 patients with pT1b RCC are shown in Table 1.

The 5-year OS rate (92.3% vs. 87.8%, p=0.501), the 5-year RFS rate (92.3% vs. 77.8%, p=0.175), and the 5-year CSS rate (92.3% vs. 94.5%, p=0.936) for the PN and RN groups showed no significant difference (Fig. 1-3).

One patient (5.5%) and 9 patients (17.3%) showed distant metastasis in the PN and RN groups, respectively. Details of distant metastasis are summarized in Table 2.

When comparing the renal function of the PN and RN groups, the proportion of patients with decreased renal function in the RN group was higher than that in the PN group (PN=0% vs. RN=11.5%). The postoperative change (1 year after nephrectomy) in the serum creatinine level was greater in the RN group than in the PN group (PN=0.2±0.2 mg/dl vs. RN=0.3±0.5 mg/dl, p=0.150). The postoperative change (1 year after nephrectomy) in the estimated GFR was also greater in the RN group than in the

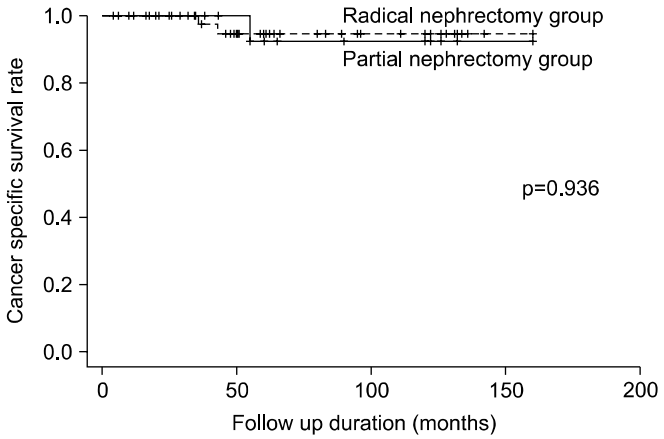

FIG. 3. Kaplan-Meier survival curve estimates of the 5-year cancer- specific survival for all patients according to whether they underwent partial nephrectomy or radical nephrectomy.

TABLE 2. Local recurrence and distant metastasis in patients with pT1b renal cell carcinoma

	Partial nephrectomy (n=18)	Radical nephrectomy (n=52)
Local recurrence	0 (0)	0 (0)
Distant metastasis	1 (5.5)	9 (17.3)
Lung	1 (5.5)	4 (7.7)
Bone	0 (0)	3 (5.8)
Liver	0 (0)	1 (1.9)
Brain	0 (0)	1 (1.9)

TABLE 3. Changes in postoperative renal function of the patients with pT1b renal cell carcinoma

	PN (n=18)	RN (n=52)	p-value[a]
Patients with increased CKD stage (n)	0	6	
Mean preoperative sCr (mg/dl)	1.0±0.2	1.0±0.2	0.782
Mean postoperative sCr (immediate) (mg/dl)	1.3±0.3	1.4±0.8	0.826
Mean postoperative sCr (after 1 year) (mg/dl)	1.2±0.2	1.3±0.6	0.460
Mean change in the sCr (after 1 year) (mg/dl)	0.2±0.2	0.3±0.5	0.150
Mean preoperative eGFR (ml/min/1.73 m^2)	86.0±20.0	81.2±19.9	0.481
Mean postoperative eGFR (immediate) (ml/min/1.73 m^2)	65.4±18.3	57.7±12.2	0.111
Mean postoperative eGFR (after 1 year) (ml/min/1.73 m^2)	73.9±12.8	63.1±16.2	0.056
Mean change in the eGFR (after 1 year) (ml/min/1.73 m^2)	12.1±9.1	18.1±12.5	0.162

PN: partial nephrectomy, RN: radical nephrectomy, CKD: chronic kidney disease, sCr: serum creatinine, eGFR: estimated glomerular filtration rate, [a]: Mann-Whitney U test

PN group (PN=12.1±9.1 ml/min/1.73 m^2 vs. RN=18.1±12.5 ml/min/1.73 m^2, p=0.162), but the difference was statistically insignificant (Table 3).

DISCUSSION

RN has generally remained the standard treatment for localized RCC for many decades because of concern about incomplete tumor excision, local recurrence, microscopic satellite tumors, and multifocality. Initially, PN was accepted as the standard treatment of only localized RCC with imperative or absolute indications (patients with a solitary kidney or bilateral RCC). The relative indications are a functioning contralateral kidney that is affected by comorbidities that might impair future renal function, such as diabetes, arterial hypertension, and arteriosclerosis, including the hereditary forms of RCC. Elective indications are those for a perfectly normal contralateral kidney [11,12].

With the widespread use of advanced diagnostic imaging techniques such USG, CT, and MRI, a large number of renal masses are being incidentally found before they produce symptoms [13]. This has led to a migration of RCC cases toward earlier stages [14]. RN has a risk of renal function deterioration. Several studies have suggested that RN is a significant risk factor for the development of chronic kidney disease. Huang et al reported that the risk of new onset of chronic kidney disease is significantly greater in patients undergoing RN than in those undergoing PN [15]. PN provides multiple options for surgically treating renal tumors [3], and during the last decade the urological community has come to accept PN as a safe, effective alternative to RN in elective situations. According to the 2007 RCC guidelines of the European Association of Urology, PN is the standard treatment for patients with clinically localized RCC $\leq$4 cm (T1a tumors) [1]. Just as PN for T1a tumors has become well accepted, physicians are now raising the issue of expanding the indications for elective PN to include larger tumors.

Several studies have suggested that the indications for PN can be safely expanded to include patients with RCC up to 7 cm (T1b tumors) [16-18]. Leibovich et al have reported 5-year CSS rates of 95% and 98% for patients with tumors measuring 4 to 7 cm and who underwent PN and RN, respectively [3]. Patard et al reported 3-year CSS rates of 98% and 97% for patients who underwent PN for tumors $<$4 and $>$4 cm, respectively [19]. These data justify the use of nephron-sparing surgery for larger, anatomically amenable tumors.

Another advantage of PN includes preservation of the maximum renal parenchyma, which help to avoid end-stage renal disease and positively impacts the quality of life [7,20]. Chronic renal failure and dialysis are associated with significant cardiovascular morbidity and mortality, and it has been suggested that RN may impact long-term survival compared with PN for renal tumors [15]. Weight et al have reported that the average excess loss of renal function observed with RN was associated with a 25% increased risk of cardiac death and 17% increased risk of death from any cause in a multivariate analysis [21]. Thompson et al reported that PN decreases the risk of chronic renal failure and complications including hip fractures and cardiovascular morbidity [22]. Lesage et al recently compared open PN and RN for renal tumors, and they concluded that the former resulted in a better quality of life due to the preservation of renal function [20]. Dash et al compared the outcomes of elective PN vs. RN for clear cell RCC 4 to 7 cm in size. They showed that renal function was better preserved after PN and that there was no clear evidence that PN was associated with an inferior oncological outcome [8]. Furthermore, the results of a recent retrospective study have shown that in selected patients with stage T1b-T3N0M0 RCC $>$4 cm in size, laparoscopic PN provides intermediate-term oncological efficacy equivalent to that of laparoscopic RN and the renal function outcomes are superior to that of laparoscopic RN [23].

In this study, PN and RN showed similar results for OS (92.3% vs. 87.8%, p=0.501), RFS (92.3% vs. 77.8%, p=0.175), and CSS (92.3% vs. 94.5%, p=0.936), respectively. Furthermore, the proportion of patients with decreased renal function (PN=0% vs. RN=11.5%) and postoperative changes in the serum creatinine level 1 year after nephrectomy (0.2±0.2 mg/dl vs. 0.3±0.5 mg/dl, p=0.150) was better in the PN group than in the RN group. Thus, our results showed

that PN is a safe and effective method for treating pT1b RCC and the oncologic and functional outcomes are good.

The limitations of this study included the retrospective nature of the analysis, the smaller number of patients in the PN group (n=18), the small numbers of oncologic events in both groups, that it was a single-surgeon experience, and the intermediate duration of follow-up. Because this was a retrospective study, the patients were not randomly assigned to a surgical procedure, which meant that the choice of surgery might have been biased by the surgeons' preference according to the preoperative condition of the patient. With time, increased patient numbers, prolonged follow-up duration, and increased numbers of events will be available for study.

Previous studies have demonstrated that for RCC >4 cm, PN has excellent survival and recurrence rates. Although PN is a controversial choice for larger tumors, we demonstrated that pT1b patients can also be treated safely and they can expect an optimal long-term oncologic efficacy with PN. Therefore, PN is effective for patients with pT1b RCC and it provides long-term tumor control while preserving renal function.

CONCLUSIONS

In this study, PN for patients with pT1b RCC had no statistically significant difference in prognosis compared with that of RN, and the renal function of the patients who underwent PN was better. PN is a feasible surgical method for treating pT1b stage RCC.

Conflicts of Interest

The authors have nothing to disclose.

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