Original Article

Renal function after nephron-sparing surgery versus radical nephrectomy in localized renal cell carcinoma (T1)

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Abstract

Objective: To evaluate renal function (GFR) after radical nephrectomy compared to partial nephrectomy in stage T1 renal cell carcinoma patients between 2005 and 2015.

Material and Method: Retrospective chart review of 409 patients who were diagnosed with renal cell carcinoma (T1) and treated with radical nephrectomy (RN) or partial nephrectomy (PN) between 2005 and 2015 (RN=136, PN=92); 228 patients with pathologically confirmed pT1 remained for analysis and were then evaluated for their estimated glomerular filtration rate (eGFR) after the surgery.

Results: There were a total of 228 (149 males and 79 females) T1 RCC patients; 136 patients were T1a with RN (57.8%) and 92 with PN (42.2%). Median follow-up was 58 months and 35 months for the RN and PN groups. From the analysis, post-operative eGFR of the RN group was decreased from 77.49 to 59.61 ml/min/1.73 m^2 and the PN group was decreased from 78.85 to 69.9 ml/min/1.73 m^2. The comparative eGFR between the 2 groups at 1 month had a significant difference (p-value<0.05). eGFR at 3 months (50.24 in RN vs 64.67 in PN), 6 months (47.98 vs 64.51), 3 years (48.79 vs 67.22) and 5 years (52.63 vs 73.59) were also significantly altered between the 2 groups. The tumor recurrence rate was not significantly different between RN and PN.

Conclusion: We found that patients treated with PN had superior post-operative renal function compared with RN. However, there was no difference in the tumor recurrence rate between the 2 groups after a follow-up of 10 years.

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Introduction

Renal cell carcinoma (RCC) is the 13th most common cancer in the world and 3rd cause of genitourinary cancers[1,2]. Radical nephrectomy (RN) has been the gold standard treatment for localized renal cortical tumors for nearly 4 decades. However, the surgical management of these tumors has evolved greatly in the past decade with the development of abdominal imaging, which can locate tumors with a great efficacy, making the surgery safer[3]. Partial nephrectomy (PN) has been introduced as the standard treatment for stage T1[4] for preserving renal function. After the operation, renal function can be assessed using serum creatinine[5,6] and the estimated glomerular filtration rate (eGFR) represents kidney damage.

According to research on renal function after nephron-sparing surgery versus radical nephrectomy: The European Organization for Research and Treatment of Cancer (EORTC) Randomized Trial 30904, the conclusion found that renal function after radical nephrectomy had decreased more than after partial surgery with a median follow-up time of 6.7 years[7].

This is the first study to report renal function data in Thailand. We investigated whether the effect of PN relative to RN on kidney function depends on baseline creatinine and oncologic outcome after surgery in stage T1 renal cell carcinoma in a series at Siriraj Hospital.

Material and Method

There was a total of 411 patients with renal cell carcinoma between 2005 and 2015; 228 patients were in stage T1 and underwent RN or PN in a single institution. The T1 RCC was divided into 2 groups. The first group was Radical with 136 patients (57.8%) and the second group was Partial with 92 patients (42.2%). The exclusion criteria were the other stages of renal cell carcinoma (T2-T4), lymph node or other distant metastasis, and a follow-up time of less than or equal 1 month.

Two outcomes for this study were collected. The primary outcome was renal function after surgery in the form of the glomerular filtration rate (eGFR). The secondary outcome was the associated factors which impacted renal function, disease-free survival (DFS), and overall survival rate.

Statistical analysis

For the characteristic data: Chi-square test and unpaired T test determined the continuous variable, and the T-test and Mann-Whitney U test were used for the single variable; multiple linear regression, Pearson correlation and unpaired T-test were used to identify associated factors influencing the differences in eGFR. All analyses were performed in SPSS V23 and p-value<0.05 was considered statistically significant.

Results

The retrospective review data had an average 58 months of monitoring time in RN and 35 months in PN. The minimum follow-up time was 1 month and the maximum 120 months in both groups; 228 patients with renal cell carcinoma in T1 were treated with elective PN (n=92) or RN (n=136). The other 183 patients were excluded from the study (Figure 1).

The preoperative characteristics of the 136 patients who underwent radical nephrectomy and the 92 patients for partial nephrectomy are provided in (Table 1). The mean patient age was 59.49±12.37 years in RN and 57.49±12.59 years in PN. The mean body mass index (BMI) was 24.98±4.27 kg/m^2 in RN and 24.86±4.088 kg/m^2 in PN. The mean tumor size was 4.4 cm and 2.9 cm from RN and PN, respectively. Patients in both groups were alike in comorbidities (ex. hypertension, diabetes mellitus (DM) type 2 or dyslipidemia). The most common histology was clear cell in 81.9% of patients, followed by papillary in 8% and the others were less than 10% (Figure 2)[9,10].

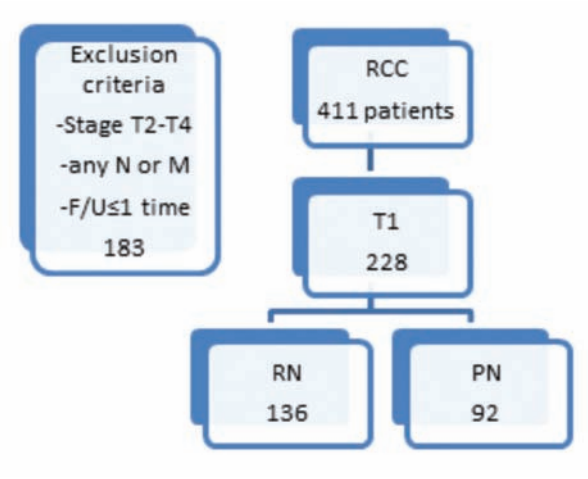

Figure 1. Consolidated standards of reporting trials diagram.

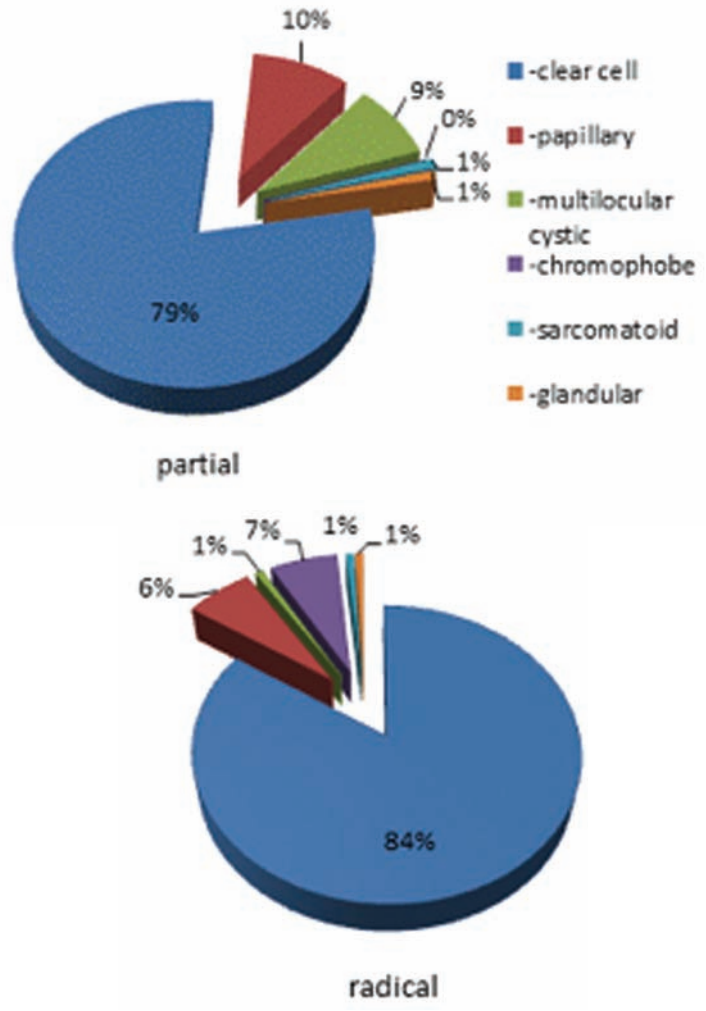

Figure 2. Pathologic cell type.

Table 1. Baseline characteristics of patients.

	Nephrectomy (N=228)		P-value
	Radical (%)	Partial (%)	
Gender			
• Male	84	65	0.166
• Female	52	27	
Chief complaint			
• Asymptomatic	84 (61.8)	70 (76.1)	
• Symptomatic	52 (38.2)	22 (23.9)	
Chronic disease			
• None	34 (25.0)	24 (26.1)	0.85
• Diabetes Mellitus	30 (22.1)	22 (23.9)	0.74
• Hypertension	83 (61.0)	50 (54.3)	0.31
• Dyslipidemia	28 (20.6)	19 (20.7)	0.99
Age (years)	59.49 ±12.37	57.49 ±12.59	0.67
Body mass index (kg/m^2)	24.98 ±4.27	24.86 ±4.088	0.96

The intraoperative and postoperative characteristics are listed in (Table 2). The mean operative time was 175 minutes in RN and 189 minutes in PN. The average blood loss was 200 ml in RN (range: 5-2300 ml) and 250 ml in PN (range: 2-2500 ml). There was no difference in time of hospitalization, average blood loss, and operative time. The mean preoperative eGFR from analysis was 77.4 ml/min/1.73 m^2 in RN and 78.8 ml/min/1.73 m^2 in PN.

There was no significant statistical difference between the groups. Post-operation: there were significant serial changes in mean eGFR at 1 month, 3 months (50.24 in RN vs 64.67 in PN), 6 months (47.98 vs 64.51), 3 years (48.79 vs 67.22) and 5 years (52.63 vs 73.59), respectively.

There were large differences in the estimated GFR between radical nephrectomy and partial that started from the 1st month (Figure 4). Time had no impact on the result; radical surgery still had a larger decrease in eGFR than partial surgery. Other associated factors found to have an effect on impaired renal function were age and DM ($p<0.05$). Hypertension, dyslipidemia and BMI do not affect post-operative GFR. Disease-free survival, from Kaplan Meier Curve, was the same between the groups, but radical surgery might be slightly better than partial surgery after 10 years of observation. We found 2 patients died from RCC out of 20 dead patients. The overall survival was 92% (Figure 5).

Complications from the operations were defined as intraoperative or post-operative within 30 days. We found complications in both groups, such as bleeding 11.8%, pleural injury 2.2%, intraabdominal organ injury 1.3% (ureteral injury, hepatic injury, small bowel injury) and arrhythmic event 1.3% (bradycardia, tachycardia, atrial fibrillation with rapid ventricular response), as shown in Table 3.

Table 2. Intraoperative and post-operative characteristics.

	Nephrectomy		P-value
	Radical	Partial	
Length of stay (days): mean±SD	7.66±2.53	7.61±2.99	0.85
Operative time (minutes): mean±SD	173.93±75.07	189.24±78.96	0.54
Estimated blood loss (ml): median (range)	200 (5-2300)	250 (2-2500)	0.15
Positive surgical margin	2 (1.5%)	1 (1.1%)	0.80
Tumor size (cm)	4.4	2.9	0.00

Table 3. Post-operative complications.

Variable	Nephrectomy		P-value
	Radical (n=122)	Partial (n=79)	
Bleeding*	14 (10.3%)	13 (14.1%)	0.379
Intraabdominal organ injury (ureter, small bowel, liver)	1 (0.7%)	2 (2.2%)	0.567
Arrhythmia event (tachycardia, bradycardia, atrial fibrillation with rapid ventricular response)	1 (0.7%)	2 (2.2%)	0.567
Pleural injury	0 (0%)	5 (5.4%)	0.006
Respiratory disease conditions	1 (0.7%)	2 (2.2%)	0.567
Fever	16 (11.8%)	14 (15.2%)	0.449

*bleeding defined as if patient receive blood transfusion.

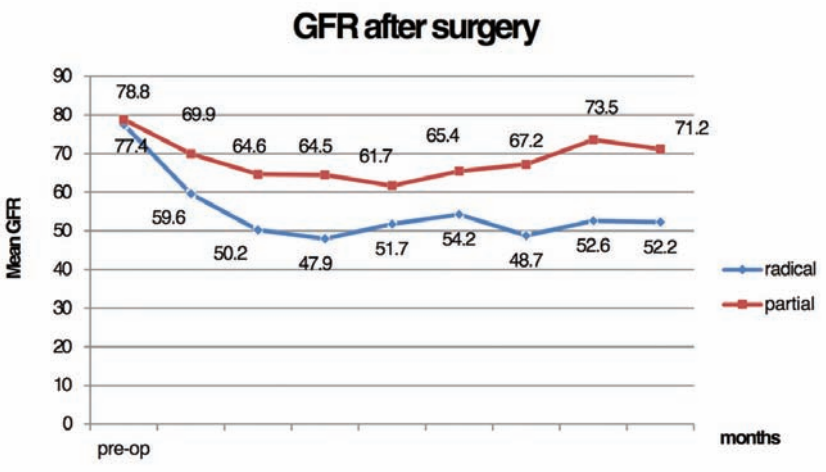

Figure 3.
Mean estimated glomerular filtration rate (eGFR) change after follow-up.

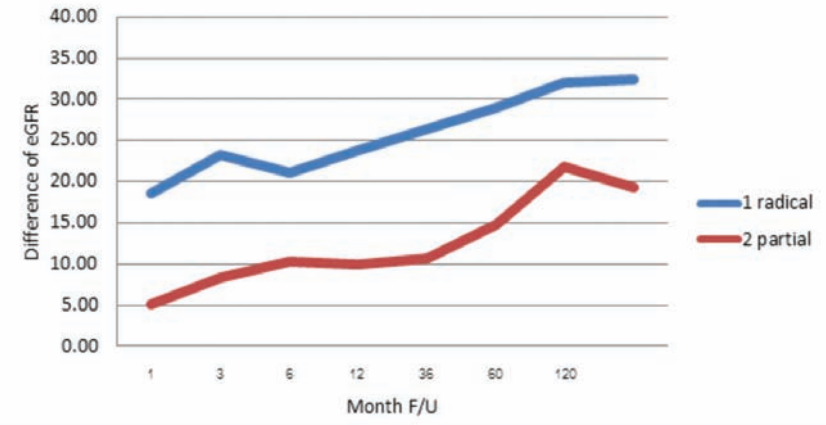

Figure 4.
Change of difference in estimated glomerular filtration rate (eGFR) between radical nephrectomy and partial nephrectomy.

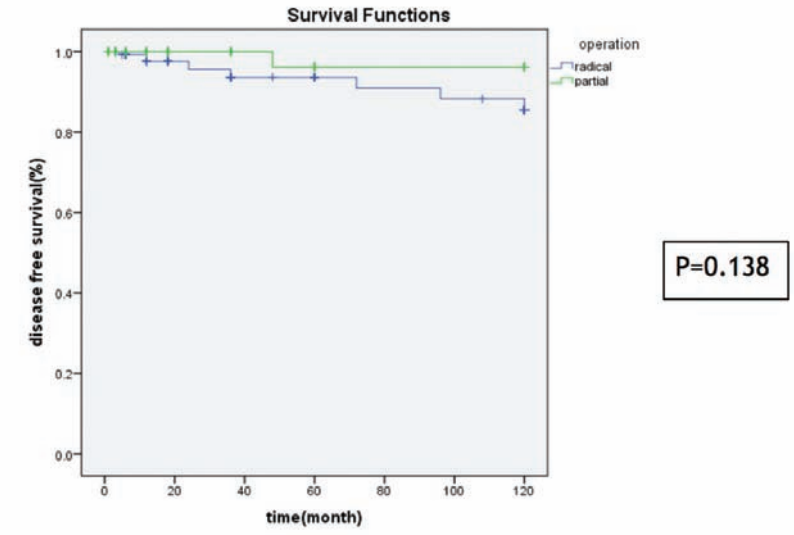

Figure 5.
Estimated disease-free survival after radical nephrectomy and partial nephrectomy by Kaplan-Meier and log rank test.

Discussion

The patient groups in our study demonstrated an average age that was around 5 decades, and greater than 70 percent of RCC were incidentally diagnosed, like in with the report from Luciani LG[8].

Nephron sparing surgery (NSS) by PN is the gold standard treatment for renal tumor T1a (<4 cm)[11] because it is the definitive surgical procedure associated with excellent oncologic and renal function outcome equal to RN[12,13]. PN is better than RN with less decrease in the postoperative glomerular infiltration rate (eGFR) and a lower incidence of CKD stage 3 or above[12]. Miller DC reported that only 20% of renal tumors 2 to 4 cm are treated with PN in the United States, and only 4% of all nephrectomies performed in England use a nephron sparing approach[14,15]. In our study about 40% underwent PN. We collected data from 2005 to 2015. There were 411 patients diagnosed with RCC and 228 patients were T1; we proceeded to operate on 136 using RN and 92 using PN (male 149, female 79).

Katsutoshi reported the time-dependent changes of eGFR after RN showed a plateau from the first postoperative day to the 60th postoperative month; PN had its lowest eGFR on postoperative day 1 and recovered to the preoperative level at 1 month[16]. Nidhi reported that GFR was 33.9% lower 3 days after PN and for the next 2-6 months was 19.7% lower than it was preoperatively[17]. Their results indicate that renal function is stable soon after RN and does not improve over the next 60 months, but that renal function improves slightly during the first month after PN. Our data: eGFR preoperative and postoperative surgery was gathered at 1 month, 3 months, 6 months, 12 months, 18 months, 3 years, 5 years, and 10 years.

Using mean eGFR calculated with the Cockcroft-Gault equation[18]. preoperative GFR was 78.8 in PN and 77.4 in RN. Postoperative at 1 month: mean eGFR decreased in both groups, from 78.8 to 69.9 in Partial and 77.4 to 59.6 in Radical. After 3 and 6 months: mean GFR also significantly decreased in Partial and Radical, and after 10 years of monitoring, we found that the mean GFR of Partial was decreased less significantly than in Radical surgery. The result of our research was the same as Dr. Katsutoshi from Japan in 2012 and Emil and Hendrik from EAU, 2013[7,16]. Also with the same change in the difference of eGFR between RN and PN, we found that in RN patients' renal function had immediately fallen after surgery at 1 month compared with PN.

Brian R. Lane indicated that the 10-year metastasis-free survival rate after PN for clinical T1a and T1b tumors was 95.2% and 90.0%, respectively; and, a minimum 5-year follow-up time was 96.9% for laparoscopic PN and 92.3% for open PN, indicating the oncologic efficacy of these 2 techniques in the hands of experienced surgeons. Although the recurrence rate was higher after OPN, these events appeared related to the greater oncologic potential of patients. This result agreed with our study's finding that the disease-free survival was 92% RN (median follow-up time 58 months) and 98% PN (median follow-up time 35 months)[19].

Historically, nephron-sparing surgery is considered to have greater morbidity than radical nephrectomy, due to the complexity of the surgery. This present study shows that there was no difference in morbidity and mortality between the 2 procedures, despite slightly higher complication rates. There was no statistically significant difference in post-operative mortality and morbidity complications between radical and partial nephrectomy. Only pleural injury was found to be higher in the Partial group.

This study has limitations due to its retrospective nature. Furthermore, it lacked randomization leading to possible selection bias of patients who underwent RN or PN. The other factor was the follow-up time: after 5yrs the number of patients decreased from loss to follow-up. The CKD equation, MDRD and serum creatinine levels are not very accurate tools for defining actual kidney function. More accurate tools are required in order to evaluate renal function,

such as 24 h creatinine clearance, serum cystatin-C or the CKD epidemiology equation (CKD-EPI)[20].

Conclusion

The serial changes in eGFR post PN were better than in RN over 10 years of monitoring. PN is the better procedure for preserving renal function in cases of small size renal cell carcinoma when compared with RN. However, they have equal efficacy for disease-free survival.

Conflict of interest

The authors declare no conflict of interest.

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