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Is partial nephrectomy worthwhile over radical nephrectomy for localised renal cortical tumours less than 7 cm in geriatric patients?

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ABSTRACT

Introduction: This study aimed to evaluate the likelihood of progression to chronic kidney disease (CKD) in a cohort of geriatric Asian patients aged over 65 years who underwent either partial nephrectomy (PN) or radical nephrectomy (RN) for localised pT1 kidney tumours.

Methods: Geriatric patients aged over 65 years who underwent PN or RN for localised kidney mass < 7 cm at a single institution from 2005 to 2014 were reviewed retrospectively. Preoperative and postoperative estimated glomerular filtration rates (eGFRs) were calculated using the Modification of Diet in Renal Disease Study equation. Clinicopathological data was analysed for new-onset CKD after at least five years of follow-up. Postoperative complications were measured by the modified Clavien classification system.

Results: Among 67 patients, 36.4% had diabetes mellitus and 80.3% had hypertension. Pre-existing CKD with $eGFR \leq 60 \text{ mL/min/1.73 m}^2$ was present in 23.3% of PN and 43.2% of RN patients. RN and PN patients had similar postoperative morbidity. Those who underwent PN had immediate decline followed by gradual improvement of their kidney functions at six months after surgery and this improvement was sustained even for patients with four years of clinical follow-up. Among patients with normal preoperative kidney functions, new-onset CKD after surgery was found in 20.0% and 52.9% of PN and RN patients, respectively ($p = 0.007$).

Conclusion: In our study, geriatric patients who underwent PN for localised kidney mass < 7 cm had immediate decline but gradual and sustained improvement in kidney functions. PN also resulted in fewer new-onset CKD through a five-year follow-up period.

Keywords: overall survival, partial nephrectomy, radical nephrectomy, renal cortical cancer

INTRODUCTION

To our knowledge, in the only prospective randomised trial to evaluate oncological outcomes between patients with partial nephrectomy (PN) and radical nephrectomy (RN) for low-stage renal cell carcinoma, the EORTC (European Organization for Research and Treatment of Cancer) Trial 30904 showed no difference in overall survival.⁽¹⁾ As for postoperative renal function, PN has been shown to reduce the risk of moderate chronic kidney disease (CKD), assuming normal preoperative kidney function.⁽²⁾ Taking reference from these two studies, we wanted to investigate whether it was still worthwhile performing nephron-saving PN for geriatric patients in Singapore.

In our study, geriatric patients were defined as individuals aged over 65 years. Geriatric patients are increasingly common in daily clinical practice, as Singapore faces an ageing population with rising life expectancy levels (mean age 82 years in 2013).⁽³⁾ The widespread use of cross-sectional imaging has also led to increased incidence of incidentally diagnosed renal tumours among elderly patients.

Current practice guidelines recommend PN for the treatment of cT1a small renal cortical tumours, whenever technically feasible, as nephron preservation has been shown to prevent the sequelae of CKD. This includes complications of anaemia, malnutrition, neuropathy, reduced quality-of-life, and increased risk of cardiovascular disease and mortality. However, with the randomised trial from the EORTC showing that there was no difference in oncological outcomes between patients undergoing PN and RN, the question of whether it was still worthwhile to perform PN for our geriatric patients assumed significance.

In clinical practice, the decision regarding treatment modality is based on thoughtful consideration of the balance to be achieved between preservation of renal function and oncologic efficacy. Our goal was thus to evaluate long-term renal and oncological outcomes for treating T1-stage renal cortical tumours among patients aged over 65 years.

METHODS

We retrospectively analysed data for 67 patients who underwent surgery for small renal cortical tumours at a single institution between 2005 and 2014, so as to achieve a minimum follow-up duration of two years.

The study received ethics approval from the institutional review board (NHG-DSRB reference 2009/00939). After ethics approval, patients who were eligible were selected for review based on the following criteria: (a) patients aged over 65 years at time of diagnosis; (b) macroscopic tumour size ≤ 7 cm; (c) had undergone either PN or RN; and (d) had organ-confined tumour, with no lymph node involvement or distant metastasis.

Patients excluded included those: (a) with repeat PN or RN for recurrences; (b) with only one solitary functioning kidney; (c) without any creatinine level measurements performed at intervals of six months, one year and two years postoperatively; (d) who had undergone radiofrequency ablation as the main therapeutic procedure. Date of last data analysis was September 2016. Patients with metastatic renal cell carcinoma were also excluded from data analysis.

The parameters analysed included preoperative patient factors, including age, ethnicity, gender, comorbidities (e.g. diabetes mellitus, last glycated haemoglobin A1c [HbA1c] level, hypertension, presence of ischaemic heart disease, American Society of Anesthesiologists [ASA] score) and haemoglobin levels, and data was collated for study. Information on tumour factors, such as tumour histological differentiation and pathological staging, was also collected. Pathological staging was performed based on the 7th edition of the American Joint Committee on Cancer classification system and histological differentiation was graded according to the Fuhrman nuclear grading system. Renal factors, such as estimated glomerular filtration rate (eGFR) measurements were estimated using the Modification of Diet in Renal Disease and Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation,⁽⁴⁾ where creatinine

levels were measured preoperatively, immediately postoperatively, and during follow-up at six months, one year, two years, three years, four years and five years. Intraoperative characteristics, such as warm ischaemia time, cold ischaemia time, total surgical time, and the presence of intraoperative and postoperative complications were also taken into account. Postoperative complications were classified using modified Clavien grading.

Due to the small number of patients in each individual subgroup, results generated from any multivariate logistic regression analysis were unlikely to be statistically significant. Hence, univariate logistic regression analysis was performed based on patients' MDRD scores and plotted over a five-year period.

The main outcome was to assess postoperative kidney function, whereby eGFR was first recorded postoperatively and subsequently at six months, one year, two years, three years, four years and five years during follow-up outpatient visits. We also took into account any new-onset CKD, as defined by the occurrence of $eGFR \leq 60 \text{ mL/min/1.73 m}^2$ on two consecutive follow-up visits at least three months apart, or by end-stage renal failure, which was defined as $eGFR < 15 \text{ mL/min/1.73 m}^2$. Besides these, overall survival, cancer-specific survival and progression-free survival were ascertained by recording patients' death status, presence of recurrence and cause of death.

RESULTS

Table I details the general demographics of our patient population in both the PN and RN groups. RN patients were associated with increased T-staging (RN 67.6%, PN 10.0%; $p < 0.001$) and higher incidence of new-onset CKD or failure (RN 52.9%, PN 20.0%; $p = 0.007$) when compared to PN patients. At baseline, there was a larger proportion of RN patients who had preoperative CKD (RN 43.2%, PN 23.3%) in comparison with PN patients. Patients in the RN group also had significantly more pre-existing comorbidities, such as diabetes mellitus (RN

44.4%, PN 26.7%) and hypertension (RN 83.3%, PN 76.7%). Postoperative complications were similar in both RN and PN patients (PN 32.1%, RN 33.3%).

Table I. Demographics and baseline clinical features of patients.

Variable	No. (%)			p-value
	Total (n = 67)	Partial nephrectomy (n = 30)	Radical nephrectomy (n = 37)	
Gender				
Women	31 (46.3)	14 (46.7)	17 (45.9)	0.953
Men	36 (53.7)	16 (53.3)	20 (54.1)	
Age (yr)*	70 (67–74)	69.5 (67–71)	71 (67–75)	0.0724
Ethnicity				
Chinese	66 (98.5)	30 (100)	36 (97.3)	< 1.000
Malay	1 (1.5)	0 (0.0)	1 (2.7)	
Diabetes mellitus				
Yes	24 (36.4)	8 (26.7)	16 (44.4)	0.135
No	42 (63.6)	22 (73.3)	20 (55.6)	
Hypertension				
Yes	53 (80.3)	23 (76.7)	30 (83.3)	0.498
No	13 (19.7)	7 (23.3)	6 (16.7)	
CKD				
Yes	21 (32.3)	7 (23.3)	14 (40.0)	0.152
No	44 (67.7)	23 (76.7)	21 (60.0)	
Stage of CKD				
Yes	23 (34.3)	7 (23.3)	16 (43.2)	0.088
No	44 (65.7)	23 (76.7)	21 (56.8)	
Estimated renal function (MDRD; mL/min/1.73 m²)[†]	71.8 ± 29.4	78.7 ± 23.2	65.8 ± 33.0	0.0775
ASA level				
2	33 (61.1)	15 (57.7)	18 (64.3)	0.619
3	21 (38.9)	11 (42.3)	10 (35.7)	
T-staging				
1a	39 (58.2)	27 (90.0)	12 (32.4)	< 0.001
1b and above	28 (41.8)	3 (10.0)	25 (67.6)	
Postoperative complications				
Yes	19 (32.8)	9 (32.1)	10 (33.3)	0.923
No	39 (67.2)	19 (67.9)	20 (66.7)	
New-onset CKD or failure				
Yes	24 (37.5)	6 (20.0)	18 (52.9)	0.007
No	40 (62.5)	24 (80.0)	16 (47.1)	

Data presented as *median (interquartile range) and †mean ± standard deviation. ASA: American Society of Anesthesiologists score; CKD: chronic kidney disease; MDRD: Modification of Diet in Renal Disease Study

Of 67 patients included in overall survival analysis, 32 patients had creatinine measurements at follow-up visits up to five years. However, 8 (11.9%) patients died before

completion of five years of follow-up, 20 (29.9%) patients were diagnosed after 2011 and hence did not have five years of follow-up data in September 2016, and 7 (10.4%) patients were lost to follow-up for other reasons.

Table II shows that average preoperative MDRD values for RN and PN patients were 65.8 ± 33.0 mL/min/1.73 m² and 78.7 ± 23.2 mL/min/1.73 m², respectively, confirming the general consensus that patients undergoing RN have poorer baseline renal functions. Average MDRD values for RN and PN patients at the five-year follow-up dropped to 42.9 ± 20.5 mL/min/1.73 m² ($p < 0.001$) and 64.1 ± 19.7 mL/min/1.73 m² ($p = 0.019$), respectively, corresponding to a 35% and 18.0% decrease in MDRD scores for RN and PN, respectively. At the five-year follow-up, 46.7% of patients who underwent PN had CKD ($p = 0.625$) when compared to 70.6% of patients in the RN group ($p = 0.125$).

Table II. Stage of CKD and renal function among patient groups.

Variable	No. (%)				p-value
	Baseline CKD		CKD at 5 yr		
	Yes	No	Yes	No	
Stage of CKD					
Partial nephrectomy	7 (23.3)	23 (76.6)	7 (46.7)	8 (53.3)	0.625
Radical nephrectomy	16 (43.2)	21 (56.8)	12 (70.6)	5 (29.4)	0.125
Estimated renal function (MDRD; mL/min/1.73 m²)*					
Partial nephrectomy	78.7 ± 23.2		64.1 ± 19.7		0.019
Radical nephrectomy	65.8 ± 33.0		42.9 ± 20.5		< 0.001

*Data presented as mean \pm standard deviation. CKD: chronic kidney disease; MDRD: Modification of Diet in Renal Disease Study

Fig. 1 shows the average MDRD values of all 67 patients across the five-year follow-up period. Both patients from RN and PN groups experienced an immediate steep decline of renal function postoperatively, with PN patients showing improved renal function at the six-month follow-up. This improvement was sustained throughout the five-year follow-up period,

as MDRD values plateaued with time. Comparatively, RN patients experienced a further decline in renal function at six months postoperatively, with no significant improvement in renal function throughout the five-year follow-up period.

To further improve the accuracy of our findings with regard to the renal functions of RN and PN patients, we further narrowed this analysis to patients who had at least four years of follow-up data (Fig. 2). A similar trend was seen among these patients ($n = 37$), as for all 67 patients, emphasising the accuracy of observations in Fig. 1.

DISCUSSION

To simplify the identification of patients with CKD, equations, such as MDRD and CKD-EPI, have been formulated to estimate eGFR. For our study, we decided to use the MDRD equation, based on the findings of Masson et al.⁽⁵⁾ In this earlier study, 825 patients were monitored for their creatinine and insulin clearance levels. Results showed that for patients with eGFR < 60 mL/min/1.73 m² and in the range 60–90 mL/min/1.73 m², MDRD showed a significantly higher accuracy of 80% when compared to accuracy of 74% using CKD-EPI. For eGFR > 90 mL/min/1.73 m², there were no significant differences between the two equations in terms of performance. As our study focused on the renal function in a Singapore geriatric population, we expected many of our patients to have pre-existing renal disease and therefore assumed that the MDRD equation would be more applicable for data analysis.

The general prevalence of diabetes mellitus and hypertension in Singapore was 11.3% and 23.5%, respectively, in 2010.⁽⁶⁾ We found that 34.3% of our patients had pre-existing CKD prior to undergoing RN and PN. It is usual for the geriatric population to have more comorbidity when compared to the general population. Accordingly, in our study, 36.4% and 80.3% of patients had diabetes mellitus and hypertension, respectively, at time of renal carcinoma diagnosis. This result significantly altered our approach towards how small renal

cortical tumours in the geriatric population should be managed, given that there is widespread evidence supporting nephropathy precipitated by diabetes mellitus and hypertension in older patients.⁽⁷⁾

In a study done by Mashni et al,⁽⁸⁾ it was demonstrated that, for patients with normal kidney function, RN was associated with a significantly higher risk for developing CKD and worse overall survival than PN, implying that PN should be the treatment of choice for nephron-sparing purposes. These authors, however, provided no details about the preoperative renal function of patients at the time of diagnosis, so that the likelihood of any patients having developed CKD prior to diagnosis of renal cancer in their cohort remained unexplored and unknown. By considering the preoperative renal function of patients and narrowing the cohort size only to geriatric patients who inherently have more comorbidities, our study demonstrated that patients who underwent PN had an immediate decline in renal function after surgery followed by gradual improvement of kidney functions by six months postoperatively, and that this improvement was sustained in patients even at the five-year follow-up visit. Comparatively, those who underwent RN showed an immediate decline in renal function after surgery that was followed by decline throughout the five years of follow-up.

Our study confirmed findings in the published literature that patients undergoing RN had significantly higher (43.2%) pre-existing CKD when compared to patients undergoing PN (23.3%). This conforms with real-life clinical practice, where surgeons are likely to recommend PN to patients who have higher viable renal function at diagnosis.

Taking reference from the EORTC randomised trial,⁽¹⁾ where there was no difference in the oncological outcomes of patients undergoing PN and RN, we set out to evaluate and compare the residual renal functions between patients in the RN and PN groups, specifically among a Singapore geriatric patient population with small renal cortical tumours. We believed

that our findings would allow urologists from Singapore to better decide on whether RN or PN would be a more appropriate procedure for their patients.

Our present study had limitations. We were unable to demonstrate any association of new-onset CKD with surgical intervention or the patient's pre-existing comorbidities. This was in spite of a majority of patients in our study having nephropathic comorbidities, such as diabetes mellitus and hypertension. Our study was mainly focused on the development of new-onset CKD and did not cover holistically other aspects of the patients' overall survival. Given that our study had a non-randomised retrospective design and was performed at a single centre, there was significant inherent bias in patient selection, as our centre does offer PN to patients with good renal function and high life expectancy. It would also have been preferable if the recurrence of disease in patients were documented in order to accurately weigh the comparative benefits and disadvantages of RN and PN.

In our study, geriatric patients who underwent PN for localised kidney mass < 7 cm had immediate decline in renal function after surgery but showed a gradual and sustained improvement in kidney functions over the five-year follow-up period. PN patients showed fewer incidence of new-onset CKD, which was also sustained throughout the five-year follow-up period. Our findings suggest that it is worthwhile to consider nephron-sparing PN for patients with small renal cortical tumours from the Singapore geriatric population, especially given that many of these patients have pre-existing comorbidities that may further worsen renal function following surgery. There is a need for future related studies, so as to more accurately demonstrate the benefits and drawbacks of PN, specifically for the Singapore geriatric population.

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FIGURE

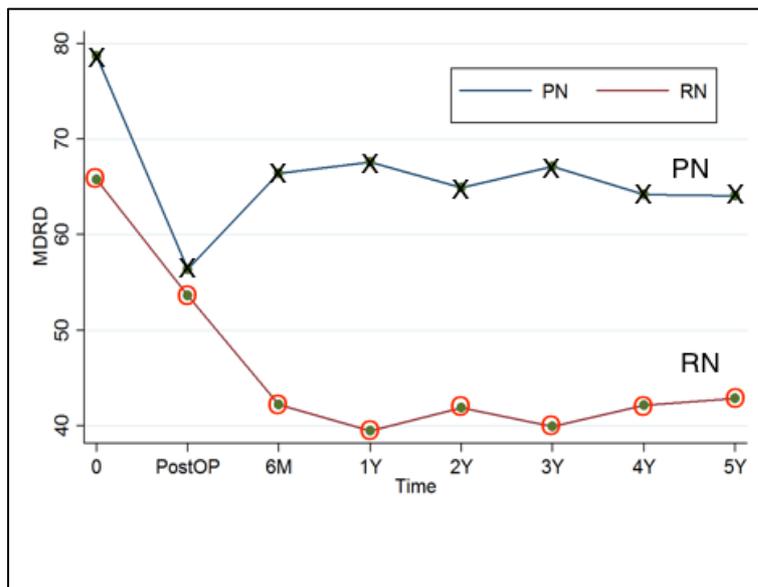


Fig. 1 Chart shows MDRD values of all patients (n = 67). MDRD: Modification of Diet in Renal Disease Study; PN: partial nephrectomy; PostOp: post operation; RN: radical nephrectomy

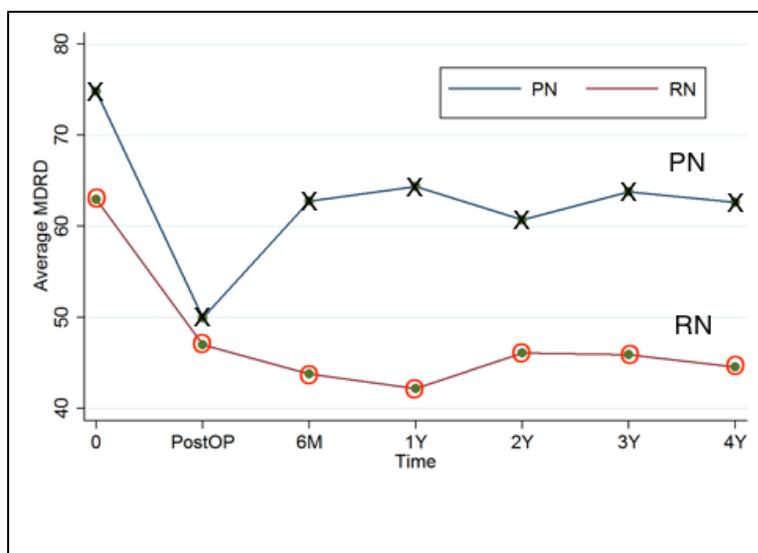


Fig. 2 Chart shows MDRD values of patients with at least four years of follow-up data (n = 37). MDRD: Modification of Diet in Renal Disease Study; PN: partial nephrectomy; PostOp: post operation; RN: radical nephrectomy