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Original article

Impact of radical nephrectomy on renal functional outcome in patients with no other co-morbidity as determined by 24-h urinary creatinine clearance



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KEYWORDS

Radical nephrectomy;
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 Renal function;
 Creatinine clearance

Abstract

Introduction: Renal cell carcinoma (RCC) accounts for 3% of all adult tumors. The mainstay of treatment of RCCs in the past has remained radical nephrectomy (RN). Studies have found a higher cumulative incidence of development of chronic renal insufficiency in patients undergoing RN for RCC.

Objectives: To determine the frequency of decrease in 24-h urinary creatinine clearance (CrCl) as an indicator of functional decline after nephrectomy for RCC.

Subjects and methods: A total of 103 patients of RCC undergoing RN were included in the study. Patients' 24-h urinary CrCls were measured pre-nephrectomy and 3 months post-nephrectomy. The patients' demographic and tumor characteristics were noted from case files. Data was analyzed by using SPSS version 15.0.

Results: There were 61 (59.2%) males and 42 (40.8%) females with a mean age of 60.12 ± 8.88 years. The mean maximum tumor diameter was 8.5 ± 2.6 cm. The mean preoperative serum creatinine in the study group was 1.01 ± 0.24 mg/dl, while the mean 3-month postoperative serum creatinine was 1.29 ± 0.46 mg/dl. The mean preoperative CrCl measured in this study was 112.02 ± 6.04 ml/min/1.73 m², while the 3-month postoperative value was 102.94 ± 14.10 ml/min/1.73 m², a mean decrease of 9.08 ml/min/1.73 m². The decrease in CrCl was identified in 34 (33%) patients. No association was found between the measured functional decline and the patients' age and gender and stage of the disease.

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Conclusion: The results from this study show that RN is associated with a decrease in CrCl in one third of the study population. Therefore it is recommended that patients undergoing RN should be strictly monitored for occult renal failure and managed promptly to prevent serious morbidity of frank renal failure.

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Introduction

Renal cell carcinoma (RCC) accounts for 3% of all adult solid tumors, with the highest incidence between 50 and 70 years of age [1,2]. With advances in radiological tools, such as ultrasound, magnetic resonance imaging (MRI) and computed tomography (CT), an increase in the detection rate of up to 40% of incidental small renal masses has been noted [3]. Radical nephrectomy (RN) has remained the cornerstone of therapy for RCC for many years. This was based on the presumption by most urologists that RN provided the excellent cancer control with little effect on the overall renal function. Most of the functional studies in the past used either serum creatinine or calculated or estimated glomerular filtration rate (eGFR) for measurement of the kidney function. Studies conducted in the recent past have shown that the renal functional outcome after nephrectomy, using serum creatinine and eGFR has underestimated the true impact on the renal function [4–7]. A recent study has shown a significantly greater decline in renal function post-RN of about 31.6% by measuring 24-h urinary creatinine clearance (CrCl) [8].

Studies have also found a higher cumulative incidence of development of chronic renal insufficiency in patients who have undergone RN [5,9]. These findings are significant as chronic renal insufficiency is associated with complications such as hypertension, anemia, malnutrition and reduced quality of life, in addition to an increased risk of cardiovascular disease and mortality [10–16].

In Pakistan, no study has been published till date, estimating the decline of renal function post-nephrectomy, especially post-RN. In this study, we studied the frequency of decrease in renal function by using 24-h CrCl in post-tumor nephrectomy so that early measures could be taken to minimize the degree of chronic renal insufficiency after tumor nephrectomy.

Subjects and methods

The study was conducted in the Adult Urology Department of Sindh Institute of Urology and Transplantation (SIUT), Karachi, Pakistan. It was a prospective cohort study. Patients' data were evaluated from July 2012 to January 2013. Patients of either gender, ≥ 18 years of age, diagnosed as RCC, on the basis of arterial enhancement on CT scan, of any stage and duration of disease were included in this study. Patients with solitary kidney, renal stones or co-morbidities like diabetes and hypertension were excluded from this study to avoid bias. Written informed consent was obtained prior to the nephrectomy and for inclusion in the study. The study was conducted according to the tenets of Declaration of Helsinki and was approved by the ethical review committee of the institute. The demographic and tumor characteristics were retrieved from the case files of patients. Patients' 24-h CrCl was measured before and 3 months post-nephrectomy according to standard methodology [8]. Renal

function was also assessed by measuring serum creatinine and eGFR using chronic kidney disease (CKD) epidemiology collaboration (CKD-epi) formula as a comparator [17].

Data analysis

The software program statistical package for social sciences (SPSS) for Windows version 15.0 (SPSS Inc., Chicago, Illinois, USA) was utilized for all statistical analysis. Mean \pm standard deviation (SD) were computed for continuous variables like age and duration of disease. Numbers and percentages were used to summarize the categorical variables like gender distribution, stage of disease and final outcome (decrease in CrCl). Stratification of data was done for age, gender, duration and the stage of disease with final outcome. The chi-square test was applied to see the association of these with the outcome variable. $p < 0.05$ was considered as significant.

Results

Between July 2012 and January 2013, 103 patients with RCC were identified who fulfilled the study inclusion criteria and were treated by RN approach. All patients were assessed for 24-h urinary CrCl before and 3 months after nephrectomy, which formed the main study variable. A decrease in the measured CrCl was the main outcome variable in the study.

The mean age of patients was 60.12 ± 8.88 years and the range was between 50 and 79 years. Sixty seven patients (65%) patients were aged ≤ 60 years while 36 (35%) were aged >60 years. Sixty-one (59.2%) patients were males, 42 (40.8%) females with the male to female ratio of 1.45:1, as shown in Table 1.

The mean maximum tumor dimension was 8.5 ± 2.6 cm. Sixty patients had a RCC of stage 2 or less, accounting for 58.3% of the study group. The rest of the 43 participants had stage 3 or higher disease, representing 41.7% of the study population. In this study, 54 of the study participants had disease duration of ≤ 6 months

Table 1 Patients demographic and tumor characteristics.

Total number of patients	103
Males	61 (59.2%)
Females	42 (40.8%)
Male to female ratio	1.4:1
Mean age (in years)	60.12 ± 8.88
Age range (in years)	50–79
Disease duration (in months)	5.58 ± 3.11
Mean maximum diameter of tumors, cm	8.5 ± 2.6
Pathologic stage of disease ≤ 2	60 (58.3%)
Pathologic stage of disease > 2	43 (41.7%)

making up 52.4% of the population. The rest of the 49 patients (47.6%) of the group had disease duration of >6 months.

The mean preoperative creatinine levels in this study group were observed to be 1.01 ± 0.24 mg/dl, while the mean postoperative value was 1.29 ± 0.46 mg/dl. The mean preoperative CrCl calculated in this study was 112.02 ± 6.04 ml/min/1.73 m², while the postoperative value was calculated to be 102.94 ± 14.10 ml/min/1.73 m². This resulted in a mean decline in measured CrCl of 9.08 ml/min/1.73 m². The final outcome of this study, i.e., decrease in CrCl, was observed in 34 (33%) of the patients.

No association was found between the measured functional decline and the patients' age (p value = 0.95), and gender (p value = 0.22) and stage (p value = 0.93) of the disease.

The mean preoperative eGFR was 96 ± 31 ml/min/1.73 m² while the mean postoperative eGFR at 3 months was 87 ± 26 ml/min/1.73 m². Thus, the renal functional assessment by calculated eGFR also complimented the findings of 24-h urinary CrCl.

Discussion

RN is considered the standard surgical approach for renal cell cancer. The CrCl measured by 24-h urine collection is considered as a standard test to assess renal function of the solitary kidney post-surgery. Improper urine collection is one of the factors that can affect the final result; nonetheless, this method is commonly used in many clinical centers and hospitals to investigate renal function. The results of the current study revealed that among the patients who underwent nephrectomy for RCC, 33% showed decreased CrCl.

RCC is a kidney cancer that originates from the lining of the proximal convoluted tubules. RCC accounts for approximately 3% of adult malignancies and 80% of neoplasms arising from the kidney [1,2]. Majority of the patients belong to old age group and male gender worldwide [3]. In this study, the majority of the patients belonged to ≤ 60 years age group (mean age of 60.12 years), with a male predominance (59.2%), with male to female ratio being 1.45:1. Out of 172 study patients, Shirasaki et al. encountered 124 (72.09%) males and 48 (27.9%) females with a mean age of 59.4 years, in their clinical study which is comparable to the results in this study [16]. Contrary to the observations made in this study, a recent study conducted in 2011 showed majority of the patients as females (69.4%) [18].

The treatment options for RCC are surgery, radiation therapy, chemotherapy, hormonal therapy, immunotherapy, or a combination of the above modalities. Among these, surgery remains the mainstay of treatment in terms of prognosis, ranging from partial (nephron-sparing), where possible, to RN depending upon the stage of disease [19]. In this study, majority of patients (58.3%) had ≤ 2 stage disease and all of them underwent RN. Generally, the widely accepted indications for nephron-sparing surgery (NSS) include tumor in a solitary kidney, bilateral renal tumors or a contralateral kidney at risk of medical disorder [16].

NSS allows maximal parenchymal preservation in cases of small renal tumors, especially those less than 4 cm in diameter. There is significantly less deterioration in total renal function in patients who are treated with partial nephrectomy than those who are treated by

RN [6,7]. It has been found that NSS is better than RN in preserving renal function even in extended warm ischemia times [13]. However, NSS still remains a grossly underutilized procedure for the treatment of renal tumors [8].

In the present study, 33% of patients exhibited decreased CrCl values after 3 months of nephrectomy, similar to previous reports, and it appears that RN has significant disadvantage on renal function. Clark et al. conducted a comparative study between partial and RN on 63 patients and observed significant postoperative change in CrCl in the RN group (31.6%) in comparison to partial nephrectomy group (6.1%) concluding that there is a significant deterioration in the overall renal function of patients who are treated with RN [8]. Similarly, Shiraski and colleagues in their prospective study to evaluate renal function post-nephrectomy too observed a number of patients having deteriorating renal functions after the surgical procedure, with 3.5% of their study population requiring hemodialysis due to poor renal functioning after nephrectomy [16].

The risk of worsening or development of de novo medical renal disease in the contralateral kidney must be considered in patients with RCC who undergo surgical removal as the primary mode of therapy. The preoperative elevated serum creatinine levels and decreased CrCls are the most important predictive factors for postoperative kidney function deterioration and are useful for screening patients who are likely to develop abnormal renal function post-nephrectomy. In such conditions, NSS can be considered nearly imperative or a relative indication in order to avoid decreases renal function [18–21].

There are certain limitations in the study too. We included only those patients who underwent RN. No comparison was made with partial nephrectomy cases, as very few partial nephrectomies are done in our set up. Renal function was measured only once after nephrectomy at 3 months. The inherent problems of compliance in 24-h urinary collection cannot be entirely excluded. We used only measured CrCl and serum creatinine as the surrogate markers of renal function and not the inulin or radionuclide based assays, which are much more sensitive and accurate. We also did not include patients with co-morbidities such as diabetes mellitus and hypertension, which might affect the rate and degree of functional decline. Our results cannot therefore be generalized to all patients. We also did not evaluate the split renal function of both kidneys; rather we used only total renal function. Nevertheless, it is the first study from Pakistan examining the effect of RN on the kidney function in the short term. More studies with larger samples and prolonged follow-up with serial determinations of renal functions are needed to validate the results of the present study.

Conclusion

In conclusion, the results from this study show that RN is associated with a decrease in CrCl in 33% of the study population. Therefore, it is recommended that patients undergoing RN should be strictly monitored for occult renal failure and managed promptly to prevent serious morbidity of frank renal failure.

Conflict of interest

None declared.

References

- [1] Latif F, Mubarak M, Kazi JI. Histopathological characteristics of adult renal tumours, a preliminary report. *J Pak Med Assoc* 2011;61:224–8.
- [2] Mohsin R, Hashmi A, Sultan G, Shehzad A, Mubarak M, Ghazanfar N, et al. Renal tumors in young adults: a single-center experience from a developing country. *Urol J* 2012;9:373–80.
- [3] Kirkali Z, Canda AE. Open partial nephrectomy in the management of small renal masses. *Adv Urol* 2008;309760.
- [4] McKiernan J, Simmons R, Katz J, Russo P. Natural history of chronic renal insufficiency after partial and radical nephrectomy. *Urology* 2002;59:816–20.
- [5] Lau WK, Blute ML, Weaver AL, Torres VE, Zincke H. Matched comparison of radical nephrectomy versus nephron-sparing surgery in patients with unilateral renal cell carcinoma and a normal contralateral kidney. *Mayo Clin Proc Mayo Clin* 2000;75:1236–42.
- [6] Matin SF, Gill IS, Worley S, Novick AC. Outcomes of laparoscopic radical and open partial nephrectomy for the sporadic 4 cm or less renal tumor with a normal contralateral kidney. *J Urol* 2002;168:1356–9.
- [7] Kim HL, Shah SK, Tan W, Shikanov SA, Zorn KC, Shalhav AL, et al. Estimation and prediction of renal functions in patients with renal tumor. *J Urol* 2009;181:2451–60.
- [8] Clark AT, Breau RH, Morash C, Fergusson D, Doucette S, Cagiannos I. Preservation of renal function following partial or radical nephrectomy using 24-hour creatinine clearance. *Eur Urol* 2008;54:143–9.
- [9] Huang WC, Levey AS, Serio AM, Synder M, Vickers AJ, Raj GV, et al. Chronic kidney disease after nephrectomy in patients with renal cortical tumors: a retrospective cohort study. *Lancet Oncol* 2006;7:735–40.
- [10] Thompson RH, Siddiqui S, Lohse CM, Leibovich BC, Russo P, Blute ML. Partial versus radical nephrectomy for 4 to 7 cm renal cortical tumors. *J Urol* 2009;182:2601–6.
- [11] Wotkowicz C, Libertino JA. Renal cell cancer: radical nephrectomy. *BJU Int* 2007;99:1231–8.
- [12] 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.
- [13] Mir MC, Takagi T, Campbell RA, Sharma N, Remer EM, Li J, et al. Poorly functioning kidneys recover from ischemia after partial nephrectomy as well as strongly functioning kidneys. *J Urol* 2014;192:665–70.
- [14] Russo P. Deleterious renal function outcomes after nephrectomy. *Eur Urol* 2011;59:340–1.
- [15] Ben-Haim S, Sopov V, Stein A, Moskovitz B, Front A, Mecz Y, et al. Kidney function after radical nephrectomy: assessment by quantitative SPECT of 99 m Tc-DMSA uptake by the kidneys. *J Nucl Med* 2000;41:1025–9.
- [16] Shirasaki Y, Tsushima T, Nasu Y, Kumon H. Long-term consequence of renal function following nephrectomy for renal cell cancer. *Int J Urol* 2004;11:704–8.
- [17] Matsushita K, Tonelli M, Lloyd A, Levey AS, Coresh J, Hemmelgarn BR, Alberta Kidney Disease Network. Clinical risk implications of the CKD Epidemiology Collaboration (CKD-EPI) equation compared with the Modification of Diet in Renal Disease (MDRD) Study equation for estimated GFR. *Am J Kidney Dis* 2012;60:241–9.
- [18] Ferreira-Filho SR, Cardoso CC, de Castro LA, Oliveira RM, Sa RR. Comparison of measured creatinine clearance and clearances estimated by Cockcroft-Gault and MDRD formulas in patients with a single kidney. *Int J Nephrol* 2011;2011:626178.
- [19] Campbell SC, Novick AC, Belldegrun A, Blute ML, Chow GK, Derweesh IH, et al. Guideline for management of the clinical T1 renal mass. *J Urol* 2009;182:1271–9.
- [20] Anderson RG, Bueschen AJ, Lloyd LK, Dubovsky EV, Burns JR. Short-term and long-term changes in renal function after donor nephrectomy. *J Urol* 1991;145:11–3.
- [21] Goldfarb DA, Matin SF, Braun WE, Schreiber MJ, Mastroianni B, Papajcik D, et al. Renal outcome 25 years after donor nephrectomy. *J Urol* 2001;166:2043–7.