Original Article

# Deterioration in the renal function and risk of microalbuminuria after radical, simple and donor nephrectomy: A long-term outcome

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## Abstract

**Objectives:** Evaluation of deterioration in renal function and risk of micro albuminuria after radical, simple and donor nephrectomy.

**Materials and Methods:** A total of 594 patients underwent nephrectomy (159 radical, 318 simple and 117 donors) from February 2009 to December 2012 in our institute. First 300 eligible patients were divided in 3 groups, each having equalled number of patients. Group 1 was consisted of patients who underwent radical, group 2 had simple and group 3 had donor nephrectomy. These patients were followed up to February 2015. Follow up of all the patients were done at first month following the surgery and then in every six months subsequently. The follow up included the measurement of serum creatinine and urinary micro albumin in a spot urine sample. CKD-EPI equation was used for calculation of e GFR.

**Results:** At the end of our study, 35 patients (41.6%) in group 1 and 8 patients (8.69%) in group 2 developed CKD stage 3. During the follow-up period, 41% patients in group 1, 13% in group 2 and 4% in group 3 developed MA.

**Conclusion:** Nephron-sparing surgery should be the standard treatment of renal tumors, wherever possible. There should be a regular follow up of the patients after radical, simple and donor nephrectomy because of risk of CKD. Early consultation with nephrologists should be done by the patients who are suffering from MA after nephrectomy.

**Key Words:** Chronic kidney disease, glomerular filtration rate, micro albuminuria, nephrectomy

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## INTRODUCTION

Radical and simple nephrectomies (SNs) are commonly performed urological procedures in cases of renal cell carcinoma (RCC) and benign renal disease, respectively. On the other hand, unavailability of cadaveric kidney donor has encouraged living donation as a source of the kidney for transplantation.[1]

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A reduction of renal mass that is a decrease in the number of nephrons is followed by a decrease in renal function. Removal of 50% of the renal mass by radical nephrectomy (RN) or live kidney donation (LKD) immediately reduces renal function to about half of its prenephrectomy value. There are functional adaptation and compensatory hypertrophy of contralateral kidney after radical or donor nephrectomy (DN).[2-5] However, in case of SN, the healthy kidney may have already undergone compensatory changes due to the diminished function of the diseased kidney.

Several studies have shown that chronic hyperfiltration, driven partly by an increase in glomerular pressure, leads to renal damage or an accelerated deterioration of preexisting renal damage.[6-12] On the other hand, multiple studies have demonstrated that LKD seems to be safe, and kidney function is well preserved in the long-term.[13-15] However, only a few studies are available regarding the changes of renal function after SN in the literature.[16-18]

It has been shown that there is a large overlap in risk factors for chronic kidney disease (CKD) and RCC, which is probably not present in the case of the benign renal disease. Therefore, many RCC patients have reduced renal function before nephrectomy and are at risk of rapid progression of end-stage renal disease postnephrectomy.[19]

Any pathology or damage to the kidney due to an acute injury can lead to proteinuria.[20] Proteinuria can be measured by 24-h urine collection or by measurement of urinary microalbumin (MA) in spot urine samples.[21] Urine MA is a known risk factor for chronic renal insufficiency.[22]

A number of studies have been done to predict the risk of deterioration of renal function after nephrectomy using preoperative variables,[23-25] but these studies had their own limitations. Therefore, we conducted this study to compare the probability of deterioration in the renal function of the contralateral kidney and risk of MA after radical, simple, and DN.

## MATERIALS AND METHODS

A total of 594 patients underwent nephrectomy from February 2009 to December 2012 in our institute. Of 594 patients, 159 underwent radical, 318 had simple, and 117 had DN. For the purpose of this study, follow-up of all the patients was done at 1$^{st}$ month following the surgery and then every 6 months subsequently.

Eligibility criteria included:

- Radiographically, normal contralateral kidney with normal preoperative serum creatinine
- Patients with one glomerular filtration rate (GFR) measurement at 1$^{st}$ month of surgery
- Urine examination negative for MA at 1$^{st}$ month of surgery
- Patients with regular follow-up after surgery.

First 300 patients eligible for the study were enrolled. Out of the 300 eligible candidates, 100 patients were allocated in each group. Group 1 consisted of patients who underwent radical, Group 2 had simple, and Group 3 had DN. Equal numbers of patients were included in each group to apply ANOVA and Tukey honest significant difference (HSD) test for statistical analysis. These patients were followed up to February 2015. The follow-up included the measurement of serum creatinine and urinary micro albumin. Spot urine sample was used for the measurement of urinary MA.

CKD-EPI equation was used for calculation of estimated GFR (eGFR) of retained kidney.[26] The CKD-EPI equation for estimation of GFR is as follows:

$$GFR = 141 \times \min(Scr/\kappa, 1)^{\alpha} \times \max(Scr/\kappa, 1)^{-1.209} \times 0.993^{Age} \times 1.018\,[\text{if female}] \times 1.159\,[\text{if black}].$$

Where Scr is serum creatinine (mg/dL), $\kappa$ is 0.7 for females and 0.9 for males, $\alpha$ is –0.329 for females and –0.411 for males, min indicates the minimum of Scr/$\kappa$ or 1, and max indicates the maximum of Scr/$\kappa$ or 1. These patients were staged according to NKF guidelines[26] after calculation of eGFR [Table 1].

Open RN was performed by anterior approach whereas flank approach was used for simple and DN.

### Statistical analyses

Analysis of GFR was done using ANOVA test. Further comparison of GFR between all the three groups was done by Tukey HSD test. Mean GFR in each group was computed separately and plotted against follow-up time. Patient's characteristics and co-morbidities were compared with the help of Z-test and *t*-test.

## RESULTS

Patient characteristics in all the three groups are reported in Table 2. Patients of Group 1 were significantly older as compared to Group 2 ($P < 0.01$). Patients suffering from hypertension (HTN) and diabetes mellitus (DM) were more frequent in Group 1 and 2 as compared to Group 3. Although, baseline GFR was higher in Group 3 as compared to Group 1 and 2, but it was statistically significant in Group 1 versus 3 ($P < 0.01$) and Group 1 versus 2 ($P < 0.05$), but it was not statistically significant in Group 2 versus 3 ($P > 0.05$).

After a follow-up of 2 years, there was statistically significant fall in GFR in Group 1 as compared to Group 2 and 3 [Graph 1]. Fall in GFR in hypertensive patients was statistically significant

in Group 1 and 2 ($P < 0.01$), but not in Group 3. Fall in GFR in the diabetic patient was statistically significant in Group 1 and 2 ($P < 0.01$). Furthermore, fall in GFR was statistically significant in patients having a smoking habit in all the three groups. But, fall in GFR in nonhypertensive, nondiabetic and nonsmoker patients was statistically significant in Group 1 only ($P < 0.01$).

Baseline CKD (i.e. eGFR <60 mL/min/1.73 m$^2$) was present in 16% of patients in Group 1 despite having preoperative normal serum creatinine.

Ten patients after a follow-up of 2 years, 13 patients after a follow-up of 4 years and 12 patients after a follow-up of 6 years developed CKD stage 3 in Group 1. Therefore, total 35 patients (41.6%) progressed to CKD stage 3 during the study period. Three patients after follow-up of 4 years and five patients after follow-up of 6 years, that is, total 18 patients (8.69%) in Group 2 developed CKD stage 3. Not even a single patient developed CKD stage in Group 3 after a follow-up of 6 years [Table 3]. Forty-one patients in Group 1, 13 patients in Group 2 and 4 patients in Group 3 developed MA during follow-up period.

**Table 1: Classification of CKD stage according to GFR**

| CKD stage | e GFR |
|---|---|
| 1 | >90 ml/min/1.73 m$^2$ |
| 2 | 60-89 ml/min/1.73 m$^2$ |
| 3 | 30-59 ml/min/1.73 m$^2$ |
| 4 | 15-29 ml/min/1.73 m$^2$ |
| 5 | <15 ml/min/1.73 m$^2$ |

**Table 2: Baseline characteristics of patients**

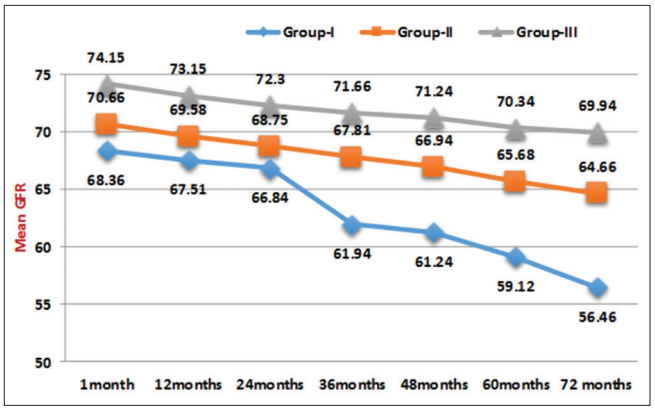
| | Group1 (RN) | Group2 (SN) | Group3 (DN) |
|---|---|---|---|
| Age (years) (Mean±Sd) | 50.07±9.66 | 43.10±3.78 | 47.43±7.41 |
| Mean baseline GFR (ml/min/1.73 m$^2$) | 68.36 | 70.66 | 74.15 |
| Male (%) | 64 | 45 | 40 |
| Female (%) | 36 | 55 | 60 |
| Hypertension (%) | 26 | 25 | 6 |
| Diabetes mellitus (%) | 9 | 6 | 0 |
| Smoking (%) | 47 | 28 | 18 |

RN: Radical nephrectomy, SN: Simple nephrectomy, DN: Donor nephrectomy

## DISCUSSION

HTN and DM have long been identified as both initiating and progressing factors in CKD, as well as, predictors of long-term renal impairment in individuals undergoing nephrectomy. Satasivam *et al.*[27] reported that patients with HTN and DM had a significantly greater percentage of reduction in postoperative GFR than those who had neither of the risk factors after RN. A study by Ito *et al.*[24] identified HTN, DM and proteinuria as significant predictors of long-term renal impairment.

Ours is the first study to report that patients even without any history of HTN, DM and smoking habit are prone for deterioration in renal function after RN. This study adds to the mounting evidence that fall in GFR was statistically significant after RN with and without co-morbidities. Hence, there are some unidentified risk factors, which are responsible for fall




**Graph 1:** Mean glomerular filtration rate of all the patients in each group according to time since nephrectomy

**Table 3: Number of patients in various CKD stages according to the time since nephrectomy**

| CKD stage | No of patients with follow up of 2 years | | No of patients with follow up of 4 years | | No of patients with follow up of 6 years | |
|---|---|---|---|---|---|---|
| | 1 month | 24 months | 1 month | 48 months | 1 month | 72 months |
| Group1 (RN) | | | | | | |
| 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| 2 | 40 | 30 | 32 | 19 | 12 | 0 |
| 3 | 6 | 16 | 9 | 22 | 1 | 13 |
| Group 2 (SN) | | | | | | |
| 1 | 1 | 1 | 1 | 1 | 0 | 0 |
| 2 | 34 | 34 | 45 | 42 | 19 | 14 |
| 3 | 0 | 0 | 0 | 3 | 0 | 5 |
| Group 3 (DN) | | | | | | |
| 1 | 0 | 0 | 2 | 2 | 3 | 3 |
| 2 | 22 | 22 | 46 | 46 | 27 | 27 |
| 3 | 0 | 0 | 0 | 0 | 0 | 0 |

RN: Radical nephrectomy, SN: Simple nephrectomy, DN: Donor nephrectomy

in GFR in patients of RCC. Further studies are necessary to find out these risk factors. Such type of renal impairment was not present after SN or DN.

A study by Huang *et al*.[28] identified that a total of 192 out of 662 patients (29%) developed a new onset of GFR lower than 60 mL/min/1.73 m$^2$ and 105 out of 662 patients (16%) developed new onset of GFR lower than 45 mL/min/1.73 m$^2$ following RN. These authors also reported that 26% of their patients had preexisting CKD (eGFR <60 mL/min/1.73 m$^2$) despite a normal serum creatinine.

At the end of our study, 35 patients (41.6%) in Group 1 and 8 patients (8.69%) in Group 2 developed CKD stage 3. A preoperative

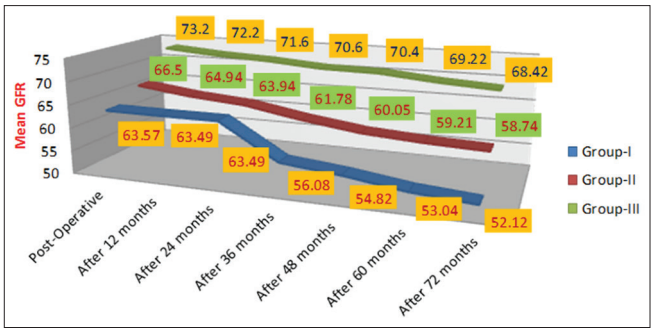
eGFR <60 mL/min/1.73 m$^2$ was present in 16% of our patients despite having normal serum creatinine. In view of this outcome, urologists should be aware of the risk of renal impairment when approaching the management of renal malignancies. Preoperative GFR should be an important part of decision making during planning of surgical treatment of RCC and overzealous use of RN should be avoided. Counseling of the patient should be done regarding the high incidence of CKD after RN and elective nephron-sparing surgery should be the standard treatment of renal tumors, wherever possible.

Increased urinary albumin excretion is a known risk factor for cardiovascular events and clinical nephropathy in patients with diabetes.[22] Viazzi *et al*.[22] study that, during long-term follow-up, microalbuminuria is a powerful predictor of chronic renal insufficiency in patients without DM and with primary HTN. In a meta-analysis, Garg *et al*.[29] concluded that the pooled risk of microalbuminuria is 3.9 after DN. A study of a large Canadian cohort demonstrated that MA is a risk factor for end-stage renal disease, even in patients whose GFR is relatively normal (>60 mL/min/1.73 m$^2$).[30]

Our study demonstrated that 41% patients in Group 1, 13% in Group 2 and 4% in Group 3 developed MA during the follow-up period. Fall in GFR was statistically significant ($P < 0.001$) in all patients suffering from MA in each group [Graph 2]. Furthermore, such quantification allows the clinician to identify those patients who would benefit from early referral to nephrologists. These patients might benefit from interventions to delay the progression of CKD, such as dietary changes, weight loss, screening for cardiovascular disease and improved control or prevention of DM and HTN.

## CONCLUSIONS

To the best of our knowledge, no study is available in the literature, in which evaluation of kidney function and




**Graph 2:** Mean glomerular filtration rate of the patients suffering from microalbumin in each group according to time since nephrectomy (significant fall $P < 0.001$)

calculation of risk of MA was done after radical, simple and DN, simultaneously. Because of the risk of CKD and MA, there should be a regular follow-up of the patients after radical, simple, and DN. Nephron-sparing surgery should be the standard treatment of renal tumors, wherever possible. Early consultation with nephrologists should be done by the patients who are suffering from MA after nephrectomy so that cardiovascular and renal complications can be avoided.

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### Conflicts of interest
There are no conflicts of interest.

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