

# Long-Term Renal Function Recovery following Radical Nephrectomy for Kidney Cancer: Results from a Multicenter Confirmatory Study



Emily C. Zabor,\* Helena Furberg, Byron Lee, Steven Campbell, Brian R. Lane, R. Houston Thompson, Elvis Caraballo Antonio, Sabrina L. Noyes, Harras Zaid, Edgar A. Jaimes and Paul Russo

From the Department of Epidemiology and Biostatistics (ECZ, HF), Renal Service, Department of Medicine (EAJ) and Urology Service, Department of Surgery (PR), Memorial Sloan Kettering Cancer Center, New York, New York, Center for Urologic Oncology, Glickman Urologic and Kidney Institute, Cleveland Clinic (BL, SC, ECA), Cleveland, Ohio, Urologic Oncology, Spectrum Health (BRL, SLN), Grand Rapids, Michigan, and Department of Urology, Mayo Clinic (RHT, HZ), Rochester, Minnesota

**Purpose:** We sought to confirm the findings from a previous single institution study of 572 patients from Memorial Sloan Kettering Cancer Center in which we found that 49% of patients recovered to the preoperative estimated glomerular filtration rate within 2 years following radical nephrectomy for renal cell carcinoma.

**Materials and Methods:** A multicenter retrospective study was performed in 1,928 patients using data contributed from 3 independent centers. The outcome of interest was postoperative recovery to the preoperative estimated glomerular filtration rate. Data were analyzed using cumulative incidence and competing risks regression with death from any cause treated as a competing event.

**Results:** This study demonstrated that 45% of patients had recovered to the preoperative estimated glomerular filtration rate by 2 years following radical nephrectomy. Furthermore, this study confirmed that recovery of renal function differed according to preoperative renal function such that patients with a lower preoperative estimated glomerular filtration rate had an increased chance of recovery. This study also suggested that larger tumor size and female gender were significantly associated with an increased chance of renal function recovery.

**Conclusions:** In this multicenter retrospective study we confirmed that in the long term a large proportion of patients recover to preoperative renal function following radical nephrectomy for kidney tumors. Recovery is more likely among those with a lower preoperative estimated glomerular filtration rate.

**Key Words:** kidney; carcinoma, renal cell; nephrectomy; creatinine; kidney function tests

## Abbreviations and Acronyms

CKD = chronic kidney disease

eGFR = estimated glomerular filtration rate

MSKCC = Memorial Sloan Kettering Cancer Center

SCr = serum creatinine

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\* Correspondence: Memorial Sloan Kettering Cancer Center, 485 Lexington Ave., 2nd Floor, New York, New York 10017 (telephone: 646-888-8299; e-mail: [zabore@mskcc.org](mailto:zabore@mskcc.org)).

PATIENTS who undergo radical nephrectomy for renal tumors are at risk for a postoperative reduction in renal function due to loss of renal mass. Previous studies have shown that lower preoperative eGFR, older

age and higher comorbidity are associated with lower postoperative eGFR and new onset CKD following radical nephrectomy.<sup>1-6</sup> It is of interest to characterize the natural history of eGFR after radical nephrectomy for

renal tumors to better understand long-term trends in renal function recovery and identify patient characteristics associated with postoperative renal function recovery.

We recently reported the results of a study investigating the postoperative natural history of eGFR in patients who underwent radical nephrectomy for kidney cancer at MSKCC and found that 49% recovered to preoperative eGFR within 2 years following surgery.<sup>7</sup> Additionally, we found that eGFR recovery differed according to preoperative eGFR. In patients with preoperative eGFR less than 60 ml/minute/1.73 m<sup>2</sup> younger age and female gender were also associated with a higher chance of eGFR recovery. In contrast, in patients with preoperative eGFR 60 ml/minute/1.73 m<sup>2</sup> or greater hypertension was associated with a lower chance of eGFR recovery and increased tumor size was associated with a higher chance of eGFR recovery.

To confirm these single center findings we performed a multicenter retrospective study using data from 3 centers where a high volume of kidney surgery is done.

## MATERIALS AND METHODS

Data were contributed by Spectrum Health, Cleveland Clinic and Mayo Clinic after institutional review board approval for retrospective data analysis. Patients from the same contemporary period who met the same inclusion and exclusion criteria as in the previous study<sup>7</sup> were selected, specifically including those with nonmetastatic renal cell carcinoma who underwent radical nephrectomy between 2006 and 2013, and had not received systemic therapy. Patients were excluded due to missing preoperative creatinine in 62, race in 47, age in 1, tumor size in 45, diabetes in 9 and no postoperative creatinine in 7. This resulted in a final sample size for this analysis of 1,928 patients with a total of 24,066 serum creatinine measurements. The final sample included 323 patients from Spectrum Health, 932 from Cleveland Clinic and 673 from Mayo Clinic.

Serum creatinine values were used to calculate eGFR using the CKD-EPI (Epidemiology Collaboration) formula,  $eGFR \text{ (ml/minute/1.73 m}^2\text{)} = 141 \times \min(\text{SCr/k, } 1)^a \times \max(\text{SCr/k, } 1)^{-1.209} \times 0.993^{\text{Age}} \times 1.018$  if female  $\times 1.159$  if black, where SCr is serum creatinine in mg/dl, k is 0.7 in female patients and 0.9 in male patients, a is  $-0.329$  in female patients and  $-0.411$  in male patients, min indicates the minimum of SCr/k or 1 and max indicates the maximum of SCr/k or 1.<sup>8</sup>

The statistical methods in this study mirrored those of the previous series,<sup>7</sup> as is common in a study attempting to confirm a previous finding. Rather than performing any variable selection or model building we simply included variables from the multivariable analysis in the prior study.

Preoperative eGFR was dichotomized as 60 or greater vs less than 60 ml/minute/1.73 m<sup>2</sup>. We plotted the trajectory of eGFR in each patient with time from the

immediate preoperative measurement through 3 years postoperatively. We used LOWESS to explore trends overall and according to dichotomous preoperative eGFR. The association of patient and disease characteristics with preoperative eGFR was analyzed by logistic regression adjusted for study center to account for possible differences across centers.

The outcome of interest in this study was postoperative recovery to preoperative eGFR within a 5% margin of error. A competing risks analysis framework was used with eGFR recovery as the primary event of interest and death from any cause as the competing event. Followup was calculated from the date of radical nephrectomy. Survivors without eGFR recovery were censored at the last eGFR measurement or 36 months, whichever was first.

The cumulative incidence of eGFR recovery was estimated. Between group comparisons were made using competing risks regression adjusted for study center. Multivariable competing risks regression was stratified by dichotomous preoperative eGFR and incorporated factors identified in our prior series, including age at surgery, gender, diabetes, hypertension and tumor size,<sup>7</sup> with additional adjustment for study center.

Statistical significance was considered at  $p < 0.05$ . All statistical analyses were performed with R, version 3.2.5 (<https://www.r-project.org/>), including the cmprsk package.

## RESULTS

Of the 1,928 patients 64.6% were male. Median age at surgery was 64 years (IQR 54–72). Median preoperative eGFR was 71.9 ml/minute/1.73 m<sup>2</sup> (IQR 56.6–87.5). Preoperative eGFR was 60 ml/minute/1.73 m<sup>2</sup> or greater in 70.1% of patients and less than 60 ml/minute/1.73 m<sup>2</sup> in 29.9%. Patients with preoperative eGFR less than 60 ml/minute/1.73 m<sup>2</sup> were older (median age at surgery 70 vs 61 years) and more of them had diabetes (27.6% vs 21.4%) and hypertension (75.6% vs 59.2%, all  $p < 0.001$ ) compared to patients with preoperative eGFR 60 ml/minute/1.73 m<sup>2</sup> or greater (table 1).

Line plots with LOWESS trends revealed that all patients experienced a decrease in eGFR immediately postoperatively followed by a generally flat trend with time in those with preoperative eGFR 60 ml/minute/1.73 m<sup>2</sup> or greater and a slightly upward trend in those with preoperative eGFR less than 60 ml/minute/1.73 m<sup>2</sup> (fig. 1, A). These trends were broadly similar to what was seen in our prior study (fig. 1, B),<sup>7</sup> although in the MSKCC data we saw a more pronounced upward trend in each group in the later part of followup.

Median survivor followup was 3.7 years (IQR 1.8–6.1). During followup 883 patients experienced recovery to preoperative eGFR and 95 died without eGFR recovery. While 499 patients recovered to within 5% of preoperative eGFR, 384 recovered to

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