Chronic Kidney Disease Due to Surgical Removal of Nephrons: Relative Rates of Progression and Survival

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Purpose: Chronic kidney disease is associated with a higher likelihood of progression to end stage renal disease and increased mortality rates. However, the etiology of nephron loss may modify the rate of chronic kidney disease progression and overall survival.

Materials and Methods: Patients with suspected renal malignancy who had a new baseline glomerular filtration rate of less than 60 ml/minute/1.73 m^2 6 weeks after surgery were divided into the 2 groups of surgically induced chronic kidney disease (preoperative glomerular filtration rate greater than 60 ml/minute/1.73 m^2) and preexisting chronic kidney disease due to medical causes followed by surgery. An independent cohort of subjects with chronic kidney disease entirely due to medical causes served as a comparator.

Results: Renal cancer surgery yielded cohorts with surgically induced chronic kidney disease (1,097) and chronic kidney disease due to medical causes followed by surgery (1,053), whereas the group with chronic kidney disease due to medical causes consisted of 42,658 subjects. The patients with chronic kidney disease due to medical causes and chronic kidney disease from medical causes followed by surgery were older compared to those with surgically induced chronic kidney disease, had more medical comorbidities and had a lower baseline glomerular filtration rate (all $p < 0.001$). The group with chronic kidney disease due to medical causes followed by surgery had a lower mean (±SD) new baseline glomerular filtration rate (37±10) compared to the surgically induced chronic kidney disease (48±9) and chronic kidney disease due to medical comorbidities (47±10) groups ($p < 0.001$). The probability of progressive decline in renal function (50% decrease in glomerular filtration rate or need for dialysis) at 3 years was lowest for surgically induced chronic kidney disease, intermediate for chronic kidney disease from medical causes followed by surgery and highest for chronic kidney disease from medical causes when age, gender, race, comorbidities and new baseline glomerular filtration rate were considered ($p < 0.001$). Nonrenal cancer related mortality was substantially lower for those with surgically induced chronic kidney disease compared to the other groups ($p < 0.001$).

Conclusions: Our data suggest that surgically induced chronic kidney disease has a lower rate of functional decline and less impact on survival than chronic kidney disease due to medical causes. These data have potential implications with respect to chronic kidney disease classification and patient counseling for surgical management of various renal disorders including renal cancer.

Abbreviations and Acronyms

CKD = chronic kidney disease

CKD-M = CKD due to medical comorbidities

CKD-M/S = CKD due to medical comorbidities followed by surgical removal of nephrons

CKD-S = CKD due to surgical removal of nephrons

eGFR = estimated glomerular filtration rate

GFR = glomerular filtration rate

PN = partial nephrectomy

RN = radical nephrectomy

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CHRONIC kidney disease is a risk factor for progression to end stage renal disease, adverse cardiovascular events and overall mortality.[1–4] Patients undergoing partial or radical nephrectomy for renal cancer experience perioperative nephron loss, which may result in de novo CKD or advancement of preexisting disease.[5–9] Postoperative renal function, typically quantified by serum creatinine, estimated/measured glomerular filtration rate or cystatin C, is a major determinant of long-term renal outcomes.[10,11] Other risk factors include structural manifestations of kidney disease such as proteinuria and the presence of systemic medical diseases such as diabetes.[12–15]

In addition, the process leading to loss of functioning renal mass (surgical vs medical) may further modify the trajectory of CKD progression in these patients. Previous reports addressing CKD progression, although robust in numbers, have been primarily limited to medical causes of CKD, and there remains considerable heterogeneity in disease progression using traditional risk factors.[1,4,16] A previous report of patients with CKD due to surgical removal of nephrons for renal cancer suggested that such patients may experience a lower rate of CKD progression and that survival in this group approximated that of patients with no CKD.[11] However, the main comparator for this analysis comprised patients with CKD due to medical causes who then required renal surgery (designated CKD-M, but in reality CKD-M/S), and a cohort of patients with CKD solely due to medical causes (true CKD-M) was not available. In addition, detailed evaluation of the impact of comorbidities and new baseline eGFR was not possible, leaving several unanswered questions. In the current study we provide a more comprehensive analysis of the rates of CKD progression and survival of patients with CKD-S compared to those with pure CKD-M as well as those with CKD-M/S.

METHODS

Study Population

This institutional review board approved analysis included adult patients who underwent renal surgery for suspected renal cancer between 1997 and 2009. Demographic, clinical and laboratory data were extracted from the Cleveland Clinic kidney surgery registry. The cohort included nephron sparing and radical nephrectomies, and the procedure choice was made by the treating surgeon based on tumor and patient characteristics. Data on patients with medical CKD were extracted from the Cleveland Clinic chronic kidney disease registry.[17] The registry was comprised of patients who had 2 estimated GFR values less than 60 ml/minute/1.73 m^2 more than 90 days apart between 2005 and 2009. We calculated estimated GFR using CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration) equations.[18]

Group Definitions

Patients with suspected renal malignancy who had a new baseline GFR of less than 60 ml/minute/1.73 m^2 within 6 weeks after surgery were divided into the 2 groups of CKD-S (surgically induced CKD, preoperative GFR greater than 60 ml/minute/1.73 m^2, new baseline GFR less than 60 ml/minute/1.73 m^2 after surgery) and CKD-M/S (preexisting CKD due to medical causes followed by surgery, ie preoperative and new baseline GFR less than 60 ml/minute/1.73 m^2). Subjects derived from the medical CKD registry constituted the CKD-M group (CKD entirely due to medical causes, no surgery involved). Patients younger than age 18 at the time of diagnosis or surgery were excluded from analysis.

Explanatory Variables and End Points

We included demographics (age, gender and race), comorbidities (hypertension, diabetes mellitus and heart disease) and renal parameters (estimated GFR and proteinuria). Baseline GFR was that measured before surgery in the CKD-S and CKD-M/S groups and at study entry for the CKD-M group. New baseline GFR was defined as the highest GFR by 42 days after surgery and was equal to baseline GFR for the CKD-M group. All subsequent serum creatinine and GFR determinations were obtained from the electronic medical record, and the latest values were used to determine latest renal function. The composite renal functional end point was time to 50% decrease in estimated GFR from postoperative new baseline GFR or institution of renal replacement therapy.[19] The mortality end points included all cause mortality and nonrenal cancer mortality.

Statistical Analysis

We present descriptive statistics as median (IQR) for continuous variables and frequency (%) for categorical variables. Wilcoxon rank sum and chi-square tests were used for between-group comparisons. We fitted postoperative new baseline estimated GFR in restricted cubic splines with 4 (5, 35, 65, 95 percentiles) knot locations to allow for flexible nonlinear associations. We assumed that incomplete data were missing at random and used multiple imputation to predict missing values of selected variables. We evaluated the relative hazard of CKD progression and mortality with CKD group using Cox proportional hazards regression. We also performed competing risk analysis to avoid the overestimation of absolute risk in the presence of competing risks. Statistical analysis was performed using SAS® (version 9.3) and the R statistical package (version 2.12.1, www.r-project.org).