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**Chronic kidney disease after radical nephrectomy for suspected renal cancers**

Yong TY *et al.* Chronic kidney disease after nephrectomy

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**Abstract**

Nephrectomy is the treatment of choice for early stage renal cell carcinoma. However, radical nephrectomy is consistently associated with higher rates of new-onset chronic kidney disease (CKD) than the general population, regardless of the method used in measuring renal function. The higher rates of CKD are associated with worsened survival because of increased risk of cardiovascular diseases and mortality. Comorbidities and adjacent non-neoplastic kidney diseases are important risk factors for the development of CKD after nephrectomy. Partial nephrectomy has become the standard of care for patients with stage 1a tumours (diameter < 4 cm) and an attractive option for those with stage 1b (diameter 4-7 cm). Therefore stratifying the risk of postoperative CKD before surgery is important and ongoing monitoring of kidney function after radical nephrectomy is needed in addition to oncological surveillance. More research is needed to better understand the risk of CKD after radical nephrectomy and develop effective strategies to optimize kidney function after such surgery.

**Key words:** Nephrectomy; Renal function; Renal cell carcinoma; Chronic kidney disease; Prevention

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**Core tip:** Chronic kidney disease (CKD) is an important complication associated with radical nephrectomy. CKD post-nephrectomy is associated with increased risk of cardiovascular diseases. Risk factors for CKD should be assessed thoroughly before radical nephrectomy. Where possible, nephron-sparing treatment should be used to mitigate the onset of CKD after tumour resection.

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**INTRODUCTION**

Renal cell carcinoma (RCC) is the third most common urological cancer but has the highest mortality rate[[1](#_ENREF_1" \o "Siegel, 2012 #84)]. The five-year survival of late stage RCC is 5%-10%[[1](#_ENREF_1)]. Radical or partial nephrectomy is the preferred treatment for the majority of patients with RCC or other renal malignancies. Although outcomes are favourable for early stage RCC treated with unilateral radical nephrectomy, concerns are emerging about the adverse impact on long-term renal function and survival. Nephrectomy for renal malignancies has been recognized as an independent risk factor for developing chronic kidney disease (CKD)[[2](#_ENREF_2),[3](#_ENREF_3)] whilst nephrectomy for other indications such as living kidney donation has a more benign long-term renal outcome[[4](#_ENREF_4" \o "Ibrahim, 2009 #3)]. CKD is defined as kidney damage for more than 3 mo (either confirmed by indicators of kidney injury such as proteinuria, or pathological disease in biopsy samples) with or without changes in estimated glomerular filtration rate (eGFR), or eGFR < 60 mL/min per 1.73 m2 for more than 3 mo[[5](#_ENREF_5)].

In the United States, 75%-80% of patients with renal cancer are diagnosed incidentally with disease localized to the kidney[[6](#_ENREF_6" \o "Jewett, 2008 #39)]. This observation is largely attributable to a 73% rise in imaging of the abdomen with CT and MRI[[6](#_ENREF_6" \o "Jewett, 2008 #39)]. In parallel with increased detection of renal neoplasms, benign renal tumours such as oncocytoma, angiomyolipoma and simple renal cysts, have been diagnosed increasingly[[7](#_ENREF_7)]. More than 20% of incidental renal masses are benign but current radiological investigations cannot accurately differentiate malignant from benign tumours[[8](#_ENREF_8" \o "Akdogan, 2012 #89)].

In this review, we will describe the epidemiology of CKD after radical nephrectomy for renal tumours and ways to prevent the development of this condition after surgery.

**EPIDEMIOLOGY**

Evidence from observational studies support the finding that radical nephrectomy is associated with higher rates of CKD, regardless of the method used in measuring renal function. Klarenbach *et al*[[9](#_ENREF_9" \o "Klarenbach, 2011 #7)] used a large Canadian population-based database of subjects who underwent nephrectomy between 2002 and 2007 to evaluate kidney outcomes after a mean follow-up of 2 years and 8 mo. Among those who underwent radical nephrectomy, 106 out of 921 (11.5%) experienced adverse renal outcomes, which was defined as end-stage renal disease (ESRD), acute dialysis, CKD (eGFR < 30 mL/min per 1.73 m2), and rapidly progressive CKD (eGFR < 60 mL/min per 1.73 m2 and eGFR loss ≥ 4 mL/min per 1.73 m2 per year)[9].

In the Memorial Sloan-Kettering Cancer Center (MSKCC) study, about a quarter of patients with T1a RCC (tumour diameter < 4 cm) had CKD (eGFR < 60 mL/min per 1.73 m2) prior to surgery despite preoperative serum creatinine within the normal range[[2](#_ENREF_2)] (Table 1). In a study of patients who had nephrectomy for T1a RCC using the linked Surveillance, Epidemiology and End Results (SEER)-Medicare database in the United States between 1998 and 2005, an increased rate of new-onset CKD was observed in patients who had radical nephrectomy (20%) compared with partial nephrectomy (11%)[[10](#_ENREF_10)]. Using data from this study, the authors estimated that the five-year rate of new-onset CKD was 18% for radical nephrectomy and 9% for partial nephrectomy.

With variable duration of follow-up after radical nephrectomy, ESRD has been reported in 0%-4% of patients in various studies[[2](#_ENREF_2),[9-11](#_ENREF_9)]. In a Canadian study involving 1151 subjects with kidney lesions who have undergone nephrectomy, 2% developed ESRD requiring dialysis within a median period of 32 months after surgery[[9](#_ENREF_9)]. However ESRD was not considered as a specific renal outcome due to its low incidence. In the SEER-Medicare (1988-2005) linked cohort, 2% of patients who had partial nephrectomy and 4% of radical nephrectomy developed ESRD when the data was censored in 2008[[10](#_ENREF_10)]. However there was no statistical difference between these two treatment groups. In the subgroup analysis of the European Organisation for Research and Treatment of Cancer (EORTC) trial, the incidence of ESRD was low in the radical nephrectomy group at 1.5% and was not significantly different from those who had partial nephrectomy[[11](#_ENREF_11)]. In the MSKCC study, none of the included subjects required renal replacement therapy, acute or chronic[[2](#_ENREF_2" \o "Huang, 2006 #1)].

Recent studies have provided new insight into differences between patients with CKD caused by medical conditions and those after nephrectomy. One study found that CKD related to nephrectomy was associated with annual kidney function decline of 0.7%, which is significantly lower than the 4.7% observed in medical-related CKD[[12](#_ENREF_12" \o "Lane, 2015 #90)].

Most studies have used either creatinine or eGFR to determine kidney function. Nonetheless serum creatinine alone does not reliably reflect kidney function due to variations in between days, extremes of age and people with different muscle mass[[13](#_ENREF_13)]. More recent studies have found that using serum creatinine and eGFR have underestimated the real effect on kidney function[[14](#_ENREF_14" \o "Kim, 2009 #43)]. By measuring 24-h urinary creatinine clearance, one study has shown a decline in renal function by 31.6% after radical nephrectomy[[15](#_ENREF_15)].

**PREDISPOSING FACTORS FOR CKD POST-NEPHRECTOMY**

Patients with renal tumours tend to be older resulting in a higher prevalence of cardiovascular diseases. As a result, this group of patients may have a greater degree of renal disease even when their creatinine concentration is still within the reference interval.

Similar systemic comorbidities and intrinsic renal risk factors might predispose people to develop both renal malignancies and CKD[[16](#_ENREF_16),[17](#_ENREF_17)]. These factors include patient characteristics (such as age, sex and ethnicity), genetic predisposition, medical comorbidities (such as hypertension, diabetes mellitus and other chronic or acute diseases), coexisting pathologies in adjacent non-neoplastic renal parenchyma and environmental exposures (such as nutrition and smoking status)[[18](#_ENREF_18),[19](#_ENREF_19)] (Table 2).

***Non-neoplastic renal parenchymal disease***

Several studies have shown that arterionephrosclerosis and glomerular diseases frequently coexist with RCC[[20-22](#_ENREF_20" \o "Bijol, 2006 #8)]. In resected tumour specimens, up to 90% have been reported to have coexisting non-neoplastic renal disease in the adjacent parenchymal tissue[[21](#_ENREF_21" \o "Henriksen, 2007 #48)]. Clinically significant intrinsic renal abnormalities, such as glomerular hypertrophy, diabetic nephropathy, mesangial expansion and diffuse glomerulosclerosis were evident in more than 60% of these specimens[[21](#_ENREF_21" \o "Henriksen, 2007 #48)].

From a study of 110 neoplasm-related nephrectomy, people with significant abnormal renal parenchyma showed a higher decrease in kidney function at 6 months after surgery in comparison to those with normal adjacent renal tissue (increase in serum creatinine by 97.24 ± 159.12 µmol/L *vs* 17.68 ± 17.68 µmol/L)[[20](#_ENREF_20)]. Nonetheless, a limitation of this study was the small sample of serum creatinine measurement on follow-up. In another study of 156 patients after tumour nephrectomy who had follow up for 12 mo or more, findings of severe arteriosclerosis or arteriolosclerosis, tubular atrophy or interstitial fibrosis, or glomerulosclerosis in nephrectomy specimens were associated with significantly lower renal function after surgery[[22](#_ENREF_22)].

One study with a follow-up of an average 19.7 mo found that after laparoscopic radical nephrectomy, the change in eGFR was significantly associated with the severity of glomerulosclerosis or the finding of interstitial fibrosis[[23](#_ENREF_23)]. For every ten percent rise in the degree of glomerulosclerosis, eGFR dropped by 9% post-surgery compared with baseline.

Another study of 65 individuals who had radical nephrectomy for RCC, elevated risk of new-onset CKD (eGFR less than 60 mL/min per 1.73 m2) was observed in association with abnormal pathology in adjacent non-neoplastic parenchyma[[24](#_ENREF_24)]. A multivariate analysis in this study showed that arteriosclerosis of more than 50% (odds ratio, OR 3.3), presence of interstitial fibrosis (OR 3.8) and glomerulosclerosis of 5% or greater (OR 3.8) were associated with significant loss in renal function after radical nephrectomy.

Findings from these studies have led the College of American Pathologists to recommend reporting of non-neoplastic renal parenchyma for examination of all tumour nephrectomy and nephroureterectomy specimens[[25](#_ENREF_25" \o "Srigley, 2010 #83)]. However, no study has reported any correlation between adjacent non-neoplastic renal disease and the development of ESRD or cardiovascular diseases after nephrectomy.

***Co-existing morbidities***

After nephrectomy, co-existing morbidities are important contributing factors to deterioration in kidney function after nephrectomy because of their effects on remaining renal parenchyma. Diabetes mellitus, hypertension and cigarette smoking have been independently linked with the decrease in renal function after nephrectomy for kidney tumours[[9](#_ENREF_9),[26](#_ENREF_26)]. These factors can lead to *de novo* development of CKD or acceleration of decline in pre-existing CKD. Studies have pointed towards a progressive increase in the risk of RCC with worsening hypertension but the pathophysiological mechanism for this relationship is still unclear[[17](#_ENREF_17),[19](#_ENREF_19),[27](#_ENREF_27)]. Diabetes mellitus is present in 6.8-23.0% of patients with RCC undergoing surgery[[27](#_ENREF_27),[28](#_ENREF_28)]. A prior diagnosis of diabetes has been found to be a predisposing factor for development of stage III CKD after radical nephrectomy[[29](#_ENREF_29" \o "Lane, 2011 #54)].

***Postoperative acute kidney injury***

Acute kidney injury (AKI) after radical nephrectomy among patients diagnosed with RCC has been found to be a significant risk factor for new-onset CKD[[30](#_ENREF_30" \o "Cho, 2011 #20)]. This study also found that about one-third of patients experienced post-operative AKI when they underwent radical nephrectomy. A year post-surgery, median GFR was lower in the AKI group compared to those without AKI. Advanced age, male gender, increased body mass index, low presurgical GFR and small size of RCC were identified as predisposing factors for postoperative AKI[[30](#_ENREF_30)]. Uncertainty remains about how these factors are associated with inadequate compensation of the remaining kidney and adaptive hyperfiltration[30]. Additional research is required to identify ways of preventing AKI after radical nephrectomy as a strategy to prevent new-onset CKD after this procedure.

***Characteristic of renal tumour***

One study has found that larger kidney tumour diameter was independently associated with decreased preoperative estimated GFR even after adjusting for hypertension and race[[31](#_ENREF_31" \o "Donin, 2012 #60)]. The findings of this study suggest that either the growth of a tumour or displacement of the non-tumour renal parenchyma affects kidney function.

On the other hand, two other studies found that small tumour size was associated with significant deterioration in renal function after radical nephrectomy[[32](#_ENREF_32),[33](#_ENREF_33)]. Therefore, researchers in these studies have advocated that partial nephrectomy are more appropriate in patients with tumour size 7 cm or less.

**POST-NEPHRECTOMY CKD, CARDIOVASCULAR DISEASES AND MORTALITY**

Higher rates of CKD in patients who had radical nephrectomy have been associated with increased risk of cardiovascular diseases and mortality[[2](#_ENREF_2),[34](#_ENREF_34)]. Using Medicare data, Huang *et al*[[2](#_ENREF_2" \o "Huang, 2006 #1)] found that the risk of cardiovascular events and non-cancer mortality was increased in the group that had radical nephrectomy. This finding was corroborated by a study from Weight and colleagues[[34](#_ENREF_34)]. In their study, they evaluated the overall and disease-specific survival in 1004 subjects with T1b RCC (tumour of 4-7 cm in diameter) who had either radical or partial nephrectomy. This study found that a significant drop in renal function was observed in those who had radical nephrectomy, over a follow-up period of 4 years. In addition, this differing rate of decline in kidney function was associated with a 25% increase in cardiovascular-related mortality and a 17% rise of all-cause mortality.

**PREVENTION OF CKD AFTER RADICAL NEPHRECTOMY**

In the past decade, partial nephrectomy has emerged as the standard treatment for most small kidney masses of less than 4 cm in size[[35-37](#_ENREF_35" \o "Patard, 2004 #64)]. Available evidence strongly supports the notion that control of cancer and risk of cancer-associated mortality for tumours up to 7 cm are not compromised by partial nephrectomy when compared with the radical procedure[[38](#_ENREF_38),[39](#_ENREF_39)].

The EORTC is the only randomized trial comparing partial and radical nephrectomy in patients with solitary kidney lesions[[40](#_ENREF_40" \o "Van Poppel, 2011 #35)]. This study randomized 541 participants with solitary renal tumours with a diameter of 5 cm or less and normal contralateral kidney to receive either radical or partial nephrectomy. After a median follow-up period of over 9 years, this trial showed an inferior outcome after partial nephrectomy in comparison with radical nephrectomy (mortality of 25.0% compared with 18.3%). However the trial closed prematurely due to low recruitment and was confounded by a large number of crossover in between the two arms of treatment.

A subsequent subgroup analysis of the EORTC study found that after a median follow-up of 6.7 years, nephron-sparing surgery was associated with a lower absolute risk (21%) of developing stage III CKD[[11](#_ENREF_11)]. In addition, stage IV and V CKD (eGFR < 30 mL/min per 1.73 m2) were observed in 10.0% of participants who had radical nephrectomy compared with 6.3% of those who had nephron-sparing surgery.

Several studies have found that partial nephrectomy can be expanded safely to patients with tumours of 4-7 cm in size (T1bN0M0)[[35](#_ENREF_35),[41-43](#_ENREF_41)]. One study has extended these findings on partial nephrectomy in patients with T1b to the population level, using analyses from the SEER registry[[44](#_ENREF_44" \o "Badalato, 2012 #26)]. Using propensity scoring, this study found no overall survival difference between partial and radical nephrectomy in a matched cohort of patients with T1bN0M0 staging. One meta-analysis of 39 studies and 41010 individuals who had surgery for small renal neoplasms found that nephron-sparing surgery had a 19% lower all-cause mortality (hazard ratio, HR 0.81; *P* < 0.0001)[[45](#_ENREF_45)]. However, this finding has to be interpreted cautiously due to the heterogeneity in study population and the inclusion of retrospective studies.

In a meta-analysis of 26 studies (27845 radical nephrectomy and 8201 partial nephrectomy), nephron-sparing surgery was associated with a 73% risk reduction of new-onset CKD (eGFR < 60 mL/min per 1.73 m2) in all included patients (HR 0.27; *P* < 0.0001) compared with radical nephrectomy[[46](#_ENREF_46)]. In patients with tumours > 4 cm, partial nephrectomy was associated with a 65% risk reduction of new-onset CKD compared to radical nephrectomy. However this systematic review was not able to assess the incidence of ESRD (eGFR < 15 mL/min per 1.73 m2) after surgery because of a lack of relevant data.

In one study, patients treated with nephron-sparing surgery have about half the risk of developing cardiovascular events compared with radical nephrectomy[[47](#_ENREF_47" \o "Capitanio, 2016 #34)]. After adjusting for clinical characteristics, comorbidities, and cardiovascular risk at diagnosis, nephron-sparing surgery was independently associated with a lower risk of cardiovascular events compared to radical nephrectomy.

However, in a meta-analysis of 6 studies (16745 radical nephrectomy and 5403 partial nephrectomy), there was no significant difference between radical and partial nephrectomy in relation to post-surgery cardiovascular events (HR 0.86; *P* = 0.24) and cardiovascular death (HR 0.71; *P* = 0.20)[[46](#_ENREF_46)]. However, these results are still contentious because of the limited number of studies.

The most likely mechanism of how partial nephrectomy confer the kidney function advantage is through preservation of a larger renal volume or some may refer to a functional volume. Among people with a single kidney undergoing nephron-sparing surgery, a larger preserved kidney volume is independently associated with better renal function[[48](#_ENREF_48),[49](#_ENREF_49)]. An increase of 5% in the volume of preserved kidney was associated with a reduction in the risk of new-onset stage IV CKD by 17%[[50](#_ENREF_50)].

After nephron-sparing surgery, the integrity and quality of the remaining parenchyma is predictive of CKD risk. In one study of 1169 subjects, a greater decline in kidney function was observed during open or laparoscopic partial nephrectomy with increased duration of warm ischaemia greater than 20 min[[51](#_ENREF_51)]. This study also showed that the duration of warm ischaemia was correlated with nadir eGFR decline after surgery and the magnitude of this reduction was associated with progression to CKD[[51](#_ENREF_51)]. Furthermore, duration of warm ischaemia of more than 25 min has been demonstrated to double the risk of severe CKD[[52](#_ENREF_52" \o "Thompson, 2010 #77)]. However, even with prolonged ischaemic time during partial nephrectomy (> 30 min), kidney function outcomes were still better than radical nephrectomy[[53](#_ENREF_53)].

Cryoablation and radiofrequency ablation are emerging as other nephron-sparing therapies for localized kidney neoplasms[[54-56](#_ENREF_54" \o "Raman, 2010 #79)]. However ablative procedure often precludes definitive pathological staging. Although a promising option for small lesions, the efficacy in terms of oncological and renal outcomes have not yet been established due to small study cohort and the absence of long-term data. Therefore surgical resection remains the preferred treatment modality in most cases of suspected kidney malignancy.

Active surveillance can be considered the preferred “nephron-sparing” procedure in patients with limited life expectancy due to comorbidities or advanced age. Lane *et al*[[57](#_ENREF_57" \o "Lane, 2010 #81)] have demonstrated that for patients 75 years or older, the renal function deterioration after radical nephrectomy is associated with higher risk of cardiovascular death. In this older age group, neither radical nor partial nephrectomy conferred a significant survival advantage over active surveillance. In the largest prospective observational study using the Delayed Intervention and Surveillance for Small Renal Masses (DISSRM) registry, the 5-year overall survival was lower in the active surveillance (75% *vs* 92%) but no difference in cancer-specific survival[[58](#_ENREF_58)].

**RISK STRATIFICATION BEFORE NEPHRECTOMY**

Comprehensive stratification of risk before nephrectomy is vital to ensure patients achieve the best functional renal outcomes. One of the risk stratification tool is the Screening for Occult Renal Disease (SCORED) which uses factors such as patient age, gender, anemia, proteinuria and cardiovascular comorbidities[[59](#_ENREF_59)]. This tool has been validated in patients with small kidney masses undergoing nephrectomy and those in the high risk category (SCORED ≥ 4) were three times more likely to develop Stage III CKD[[60](#_ENREF_60)]. Another group has proposed an alternative instrument for risk prediction. Sorbellini *et al*[[61](#_ENREF_61)] have devised a nomogram to predict decline in kidney function, which was defined as two or more creatinine measurements of 176 µmol/L within a month after surgery. This nomogram takes into account the change in kidney volume and pre-surgery creatinine but does not include preoperative comorbidities which can be important risk factors for CKD.

Other models of risk prediction have used information from renal parenchyma surrounding the tumour[[23](#_ENREF_23)]. The presence and extent of glomerulosclerosis in adjacent parenchyma has been found to correlate with decline in kidney function after nephrectomy but this relationship is not observed with arteriosclerosis, interstitial fibrosis or tubular atrophy[[23](#_ENREF_23)]. Brandina *et al*[[24](#_ENREF_24)] have proposed a nomogram using age-adjusted Charlson comorbidity index, percentage of glomerulosclerosis in the adjacent non-neoplastic parenchyma and baseline eGFR before surgery to predict the probability of developing CKD after nephrectomy. However this nomogram has not been validated for clinical use.

**KNOWLEDGE GAP AND FUTURE RESEARCH**

The evidence to support nephron-sparing surgery in patients with suspected RCC has been derived mainly from single-centre cohort studies. Consequently these studies lack standardisation in the definition for renal impairment, method in assessing kidney function and varying cutoff or stages of CKD as the primary outcome. Furthermore there is also disparities between studies in terms of eligibility criteria and duration of follow-up after surgery.

Hitherto, none of the studies have used ESRD after nephrectomy as the primary endpoint. Future work is needed to evaluate the effects of nephrectomy on patients, particularly with ESRD as the main endpoint, and the possible two-way relationship between RCC and CKD. Further research is required to better understand how CKD develops or progresses after nephrectomy and identify effective measures to prevent CKD and associated adverse effects in this setting. While comorbidities such as hypertension and diabetes mellitus are cited as risk factors for new-onset CKD or worsening kidney function after radical nephrectomy, no study have evaluated how interventions to control these risk factors may potentially influence outcome.

Assessment of kidney function before and after nephrectomy is still largely based on serum creatinine measurement. Although serum cystatin C has been found to be a good predictor of AKI in different settings[[62-64](#_ENREF_62" \o "Zhang, 2011 #95)], its use has not been evaluated in those undergoing nephrectomy. Similarly, another marker, neutrophil gelatinase-associated lipocalin (NGAL), has not been studied in patients having nephrectomy.

The increased incidence of CKD after radical nephrectomy also highlights the need for more research to distinguish between high- and low-risk renal tumours before surgery to better select patients who will require surgical management. Clinical trials are currently investigating gene alterations such as chromatin remodelling and microsatellite instability as tool for such differentiation (NCT02204800 and NCT01305330). Urinary biomarkers such as aquaporin-1 and perilipin-2 have demonstrated early promise in differentiating benign tumours from malignant RCC[[65](#_ENREF_65" \o "Morrissey, 2015 #100)]. Newer markers such as decreased expression of small non-coding RNAs known as PIWI-interacting RNAs have also been associated with poor survival in RCC[[66](#_ENREF_66)]. However more research is required to validate the accuracy of these markers in the pre-surgical diagnosis of RCC.

Future studies are needed to address a number of important gaps in knowledge for patients who had radical nephrectomy. Table 3 summaries a few key questions about kidney function and adaptation after radical nephrectomy that warrants further research.

**CONCLUSION**

Consistently, patients who have undergone radical nephrectomy for a suspected kidney malignancy are at increased risk of CKD. The concern with the deterioration in kidney function after radical nephrectomy is that this group of patients are at increased risk of ESRD and adverse cardiovascular outcomes. Coexisting medical disorders including diabetes mellitus, hypertension and abnormalities in the remaining kidney parenchyma are risk factors for new-onset CKD after radical nephrectomy. A comprehensive assessment of developing CKD after radical nephrectomy should be undertaken in every patient in whom this procedure is being considered so that management decisions can be better informed.

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**Table 1 The incidence or prevalence of chronic kidney disease or end-stage renal disease before and after radical or partial nephrectomy for suspected renal cancers**

|  |  |  |
| --- | --- | --- |
| **Population** | **Incidence or prevalence** | **Ref.** |
| CKD in patients with T1a RCC before surgery | 26% | Huang *et al*[[2](#_ENREF_2)] |
| New-onset CKD after radical nephrectomy (SEER-Medicare database) | 20% | Sun *et al*[[10](#_ENREF_10)] |
| New-onset CKD after partial nephrectomy (SEER-Medicare database) | 11% | Sun *et al*[[10](#_ENREF_10)] |
| ESRD after radical nephrectomy | 2%-4% | Sun *et al*[[10](#_ENREF_10)]Scosyrev *et al*[[11](#_ENREF_11)] |
| ESRD after partial nephrectomy | 2% | Sun *et al*[[10](#_ENREF_10)] |

CKD: Chronic kidney disease; ESRD: End-stage renal disease; RCC: Renal cell carcinoma; SEER: Surveillance, Epidemiology and End Results.

**Table 2 Risk factors associated with new-onset chronic kidney disease or acceleration of pre-existing chronic kidney disease after radical nephrectomy**

|  |  |  |
| --- | --- | --- |
| **Risk factor** | **Odds ratio (95%CI); *P*-value** | **Ref.** |
| Diabetes mellitus | 11.60 (1.39-97.04); *P* = 0.024 | Brandina *et al*[[24](#_ENREF_24)] |
| 2.74 (1.07-6.98); *P* = 0.035 | Cho *et al*[[30](#_ENREF_30)] |
| Hypertension | 3.67 (1.28-10.48); *P* = 0.153 | Brandina *et al*[[24](#_ENREF_24)] |
| Low preoperative GFR (< 90 mL/min per 1.73 m2) | 3.30 (1.16-9.37); *P* = 0.025 | Brandina *et al*[[24](#_ENREF_24)] |
| Preoperative GFR (per 10 mL/min per 1.73 m2 rise) | 0.47 (0.36-0.60); *P* = 0.0001 | Cho *et al*[[30](#_ENREF_30)] |
| Postoperative AKI | 4.24 (2.28-7.89); *P* = 0.0001 | Cho *et al*[[30](#_ENREF_30)] |
| Adjacent non-neoplastic kidney parenchyma abnormalities |  |  |
| Arteriosclerosis > 50% | 3.33 (1.03-10.79); *P* = 0.045 | Brandina *et al*[[24](#_ENREF_24)] |
| Interstitial fibrosis (present) | 3.78 (1.32-10.76); *P* = 0.013 |
| Glomerulosclerosis ≥ 5% | 3.78 (1/24-11.50); *P* = 0.0061 |

AKI: Acute kidney injury; GFR: Glomerular filtration rate.

**Table 3 Questions to be addressed by future studies**

How is long-term cardiovascular health affected by radical nephrectomy?

What is the incidence of end-stage renal disease and renal replacement therapy after radical or partial nephrectomy?

What reliable investigations can be used to identify patients with renal cell carcinoma prior to surgery?

How does the contralateral kidney compensate after radical nephrectomy?

How can kidney function be preserved after nephrectomy?