Renal and Cardiovascular Morbidity After Partial or Radical Nephrectomy

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For this study, the linked Surveillance, Epidemiology, and End Results (SEER)-Medicare database was used. The interpretation and reporting of these data are the sole responsibility of the authors.

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BACKGROUND. To clarify the benefits of nephron-sparing surgery among patients with early-stage kidney cancer, the authors compared the frequency of renal and cardiovascular morbidity after partial or radical nephrectomy.

METHODS. This retrospective cohort study was based on linked Surveillance, Epidemiology, and End Results-Medicare data. The authors identified 10,886 patients who underwent partial or radical nephrectomy between 1991 and 2002. Medical claims were examined for the occurrence of adverse renal and/or cardiovascular outcomes, and multivariate survival models were fit to estimate the association between type of surgery and each clinical outcome, using propensity scores to balance the treatment cohorts with respect to measured patient and disease characteristics. To control for secular trends in the indications for partial nephrectomy, separate analyses were performed based on treatment era (1991–1999 or 2000–2002).

RESULTS. During the study interval, 10,123 patients (93%) and 763 patients (7%) underwent radical or partial nephrectomy, respectively. During 2000 to 2002, patients who underwent partial nephrectomy experienced fewer adverse renal outcomes (16.4% vs 21.8%; adjusted hazard ratio, 0.74; 95% confidence interval, 0.58-0.94), including a trend toward less frequent receipt of dialysis services, dialysis access surgery, or renal transplantation. The likelihood of adverse cardiovascular outcomes did not differ by treatment.

CONCLUSIONS. Among contemporary patients, partial nephrectomy was associated with less clinically apparent renal morbidity than radical nephrectomy. This finding motivates expanded use of partial nephrectomy among patients with early-stage kidney cancer. Given the potential for selection bias and residual confounding in this observational cohort, additional prospective studies will be necessary to validate the current findings. ***Cancer* 2008;112:511–20.** © *2007 American Cancer Society.*

KEYWORDS: kidney cancer, renal cell carcinoma, surgery, partial nephrectomy, radical nephrectomy, morbidity, cardiovascular.

Radical nephrectomy is the traditional gold-standard treatment for patients with early-stage kidney cancer. Greater than 2 decades ago, urologists introduced partial nephrectomy as a technically feasible, nephron-sparing alternative.[1] On the basis of concerns about local recurrence, surgeons initially reserved partial nephrectomy for patients with mandatory or relative indications for nephron-sparing surgery, such as bilateral tumors, tumor(s) in a solitary kidney, pre-existing chronic kidney disease, and/or medical comorbidities that threaten future renal function.[2]

In the late 1990s, data describing cancer control outcomes equivalent to those for radical nephrectomy began to appear in the literature.[3–6] Clinicians subsequently broadened the indications for

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partial nephrectomy to include its elective application among the growing pool of patients with small (≤4 cm), incidentally detected renal masses and a normal contralateral kidney. In the elective setting, partial nephrectomy offers the unique benefits of better preserving long-term renal function[7–10] while simultaneously reducing over treatment of benign[11] or clinically indolent[12] tumors.

Nonetheless, radical nephrectomy remains the predominant surgical therapy for patients with early-stage kidney cancer, including those with small tumors.[13,14] This trend may reflect lingering skepticism regarding the relative advantage of elective partial nephrectomy.[15] Although postoperative glomerular filtration rates are higher among patients who undergo elective partial nephrectomy,[7–9] it remains unclear whether this predicts reductions in clinically apparent renal morbidity. Moreover, despite an established association between impaired renal function and adverse cardiovascular health outcomes,[16,17] differences in cardiovascular morbidity after treatment with partial versus radical nephrectomy have not been confirmed empirically.

We hypothesized that clinically apparent adverse renal and cardiovascular outcomes are less frequent after elective partial nephrectomy than after radical nephrectomy. To test this hypothesis, we compared the frequency of postoperative renal and cardiovascular morbidity among a population-based cohort of Medicare beneficiaries who underwent partial or radical nephrectomy for newly diagnosed kidney cancer. In the absence of clinical trials comparing such outcomes after partial or radical nephrectomy, these observational data clarify the potential benefits of nephron-sparing surgery and inform ongoing efforts to define optimal kidney-cancer treatment algorithms.

MATERIALS AND METHODS

Analytic Framework

We hypothesized that the clinical indications for partial nephrectomy demonstrated secular trends during the study interval. We specifically posited that, before 2000, most patients who underwent partial nephrectomy had mandatory or relative indications (eg, preexisting renal insufficiency or diabetes mellitus) for nephron-sparing surgery. Therefore, patients who underwent partial nephrectomy during the period from 1991 to 1999 were systematically at greater risk than patients who underwent radical nephrectomy for the development of adverse postoperative renal and cardiovascular outcomes. We further hypothesized that in 2000 and thereafter—after the publication of long-term data supporting the oncologic equivalence of partial and radical nephrectomy for patients with small renal tumors[3–6,18]—the use of partial nephrectomy no longer was restricted to those patients at heightened risk for development of chronic kidney disease. Instead, most patients who underwent partial nephrectomy after the millennium had elective nephron-sparing surgery. Thus, given the potential for confounding by indication, we decided a priori to perform separate analyses based on treatment era (ie, 1991–1999 and 2000–2002).

Data Source

We used linked data from the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) Program and the Centers for Medicare and Medicaid Services (CMS) to identify and characterize a cohort of older patients (aged ≥66 years) with incident kidney cancer diagnosed from 1991 through 2002. Medicare claims for this cohort are available through December 31, 2003. Accordingly, this date represents the end of our follow-up interval.

SEER is a population-based cancer registry that collects data regarding incidence, treatment, and mortality. The demographic composition, cancer incidence, and mortality trends in the SEER registries are representative of the entire United States population.[19]

From 1991 through 1999, 11 SEER-affiliated registries (San Francisco, San Jose [1992], Los Angeles [1992], Connecticut, Detroit, Hawaii, Iowa, New Mexico, Seattle, Utah, and Atlanta) provided incident cases for linkage with healthcare claims covered by the CMS. In 2000, the SEER-Medicare dataset expanded to include patients from the Greater California, Louisiana, New Jersey, and Kentucky tumor registries. The Medicare program provides primary health insurance for 97% of the United States population ages ≥65 years. Successful linkage with CMS claims is achieved for >90% of Medicare patients whose cancer-specific data are tracked by SEER.[20]

Cohort Identification

We identified a preliminary cohort of 13,247 Medicare beneficiaries who were diagnosed between 1991 and 2002 with localized/regional, nonurothelial kidney cancer (information available from the authors upon request). For each patient, we searched the inpatient Medicare file (Medicare Provider Analysis and Review) for *International Classification of Diseases, 9th Revision, Clinical Modification* (ICD-9) claims that specified a hospital admission during which the patient underwent surgical treatment with either radical nephrectomy (ICD-9 codes 555 and 5551) or partial nephrectomy (ICD-9 code 554).

Of these patients, we excluded 2285 who lacked the specified claims denoting surgical treatment for kidney cancer. We also excluded 76 patients whose claims suggested the presence of bilateral tumors at diagnosis. This yielded a final analytic cohort of 10,886 patients (82.2% of the preliminary cohort) with Medicare claims that specified treatment with partial or radical nephrectomy.

Patient Characteristics

We used SEER variables to ascertain demographic and cancer-specific information (ie, age at surgery, sex, race/ethnicity, marital status, United States Census region, year of surgery, tumor size, tumor stage, tumor grade) for each patient in the analytic cohort. Because complete data for 2003 were not available, we assigned 2002 as the year of surgery for the 101 patients who were diagnosed in 2002 but underwent surgery in 2003. We collapsed tumor size into 2 clinically relevant categories based on a 4-cm threshold.[4] We assigned median Census-tract income and Census-tract percentage of nonhigh-school graduates as patient-level measures of income and education, respectively.[21]

We measured pre-existing comorbidity using a modification of the Charlson index[22] by identifying comorbid conditions (which included diabetes, renal insufficiency, and cardiovascular disease) from inpatient and physician claims that were submitted during the 12-month period before the index admission for kidney cancer surgery.[23] We also noted the presence or absence of hypertension, urolithiasis, and/or renovascular disease given their relevance to surgical decision-making among patients with kidney cancer.

Outcome Measures

We drew on the existing literature[16,24–27] to guide specification of medical claims-based definitions for the following renal health outcomes: 1) hospitalization for or diagnosis of chronic renal insufficiency or end-stage renal disease (ESRD), 2) nephrology consultation, 3) receipt of physician services for ESRD, 4) dialysis access surgery, 5) hemodialysis or peritoneal dialysis, and 6) renal transplantation. For analytic purposes, we consolidated these into 2 primary (nonmutually exclusive) renal outcomes: 1) any adverse clinical renal outcome and 2) receipt of dialysis services or transplantation (information available upon request). To avoid the detection of surgical complications, we evaluated only those claims that were submitted from 30 days after the index cancer surgery through the end of our follow-up interval (December 31, 2003).

We used claims-based definitions for 2 cardiovascular outcomes associated with chronic kidney disease[16,17,26]: 1) ischemic heart disease-related hospitalizations or diagnoses and 2) congestive heart failure-related hospitalizations or diagnoses (information available upon request). For analytic purposes, we consolidated these into a single primary cardiovascular outcome ('any postoperative cardiovascular morbidity') (information available upon request). We evaluated only those claims that were submitted from 30 days after the index cancer surgery through the end of our follow-up interval (December 31, 2003).

In a secondary analysis, we examined the association of surgical therapy with cause-specific and overall survival. We hypothesized that cause-specific and overall mortality would not differ between treatments. We ascertained the occurrence of death from any cause ($\geq$30 days after the index surgery) based on the date of death provided by CMS. We defined overall survival as the interval from the date of surgery to the date of death. We used the cause-of-death variable from SEER to identify kidney-cancer-attributable deaths.

Statistical Analysis

We used chi-square tests to evaluate the association between surgery type and various demographic and cancer-specific variables and to assess temporal changes in the use of partial nephrectomy. We undertook a 2-step approach for multivariate analyses. First, because patients were not randomized to undergo partial or radical nephrectomy, we used propensity scoring techniques to limit the influence of selection bias on treatment outcomes.[28,29] Given our interest in time-to-event outcomes, we then fit multivariate survival models to estimate the association between surgery type and our renal, cardiovascular, and survival outcomes.

Propensity Scores

We used propensity scores to balance the partial and radical nephrectomy cohorts with respect to observed patient and disease characteristics. The propensity scores reported herein represent each individual's probability of receiving a partial nephrectomy, conditional on known demographic and disease-specific characteristics. To calculate the propensity scores, we fit logistic regression models with receipt of partial nephrectomy (yes/no) as the outcome variable and the predictor variables of age, race/ethnicity, United States Census region, education, income, tumor size, tumor stage, tumor grade, and pre-existing comorbidity (Charlson index score, hypertension, urolithiasis, and renovascular disease).

We then sorted our sample into 10 equal-sized strata based on predicted probabilities (ie, propensity scores) of receiving a partial nephrectomy. We used chi-square and *t* tests to assess for covariate balance (between treatment groups) within each stratum.

Survival Analyses

After confirming covariate balance within propensity score strata, we fit Cox proportional hazards models for our primary renal and cardiovascular outcomes and for the disease-specific and overall mortality endpoints. We performed separate analyses for the 2 treatment eras. For each model, we included indicator variables for 9 of the 10 propensity score strata and for treatment group (ie, partial vs radical nephrectomy).[30] To account for residual selection bias, we also adjusted our models for each variable that contributed to propensity score estimation.[28,29]

We checked the proportional hazards assumption by adding time-dependent variables (ie, covariate*-log[time]) to the model and verifying an absence of statistical significance. On the basis of this step, we noted violation of the proportional-hazards assumption for the overall and disease-specific survival models. Accordingly, for these 2 outcomes, we fit stratified proportional hazards models. The stratified disease-specific survival model for patients who were treated before 2000 failed the proportional-hazards assumption, leading us to fit a parametric survival model for this outcome.

In a sensitivity analysis, we fit survival models that included only propensity score strata and treatment indicator variables (without additional adjustment for the independent variables that contributed to propensity score estimation). Because pathologic tumor stage and grade typically are unknown at the time of treatment choice, we also repeated our multivariate analyses after estimating propensity scores without stage and grade as predictor variables. All statistical testing was 2-sided and was carried out at the 5% significance level in SAS (version 9.1; SAS Institute, Cary, NC).

RESULTS

Study Cohort

Our analytic cohort comprised 10,886 Medicare beneficiaries who underwent surgery for a kidney cancer diagnosed between 1991 and 2002. Among this cohort, 10,123 patients (93%) underwent radical nephrectomy, and 763 patients (7%) underwent partial nephrectomy. Table 1 presents demographic and clinical characteristics of the analytic sample stratified by treatment group. Patients who underwent partial nephrectomy differed in age; sex; treatment era; tumor size, stage, and grade; and prevalent hypertension ($P < 0.05$) (Table 1). Figure 1 depicts the annual number and proportion of patients who underwent partial nephrectomy.

Table 2 illustrates the distribution of key confounders, which was similar within propensity score strata for patients who underwent partial or radical nephrectomy; none of the residual differences were statistically significant. Thus, the treatment groups were balanced with respect to tumor size (ie, the percent of patients with tumors ≤4 cm) and other clinically relevant variables.

Survival Analyses

By the end of the study interval, 2854 patients (25.4% of the total sample) developed at least 1 adverse renal outcome, and 676 patients (6.0%) received renal dialysis or transplantation services. Table 3 presents the frequency of adverse renal outcomes for patients who underwent partial or radical nephrectomy stratified by treatment era. Among patients who were treated from 1991 to 1999, the likelihood of experiencing any adverse renal outcome or requiring dialysis/transplantation-related services did not differ by surgery type (Table 3). In contrast, treatment with partial nephrectomy from 2000 to 2002 was associated with a reduced likelihood of developing any adverse renal outcome (16.4% vs 21.8%; adjusted hazard ratio [HR], 0.74; 95% confidence interval [95% CI], 0.58–0.94) and a trend toward less frequent receipt of postoperative dialysis and/or transplantation services (2.7% vs 4.7%; adjusted HR, 0.58; 95% CI, 0.33–1.04) (Table 3).

Adverse cardiovascular outcomes occurred commonly (6530 patients; 60% of the total sample) but did not differ in frequency between treatment groups in either era (Table 3). For the renal and cardiovascular outcomes, we reached the same conclusions based on Cox models that were adjusted only for propensity score strata indicator variables. Likewise, our findings did not change substantively when the propensity score estimates did not account for tumor stage or grade.

During the study interval, 5201 patients died, and 1545 of those deaths (29.7%) were attributed to kidney cancer. Among patients who were treated from 2000 to 2002, partial nephrectomy was associated with a reduced risk of death from any cause (adjusted HR, 0.72; 95% CI, 0.56–0.92). Kidney cancer-specific survival did not differ by treatment group (data not shown).

TABLE 1
Patient Characteristics According to Receipt of Radical Versus Partial Nephrectomy

	No. of patients (%)		
Characteristic	Radical nephrectomy	Partial nephrectomy	P*
Total	10,123 (93)	763 (7)	
Mean age at surgery [SD], y	74.7 [6]	73.4 [5.5]	<.001
Year of surgery			<.001
1991–1999	5701 (95.3)	280 (4.7)	
2000–2002	4422 (90.2)	483 (9.8)	
Sex			.036
Men	5762 (92.6)	464 (7.4)	
Women	4361 (93.6)	299 (6.4)	
Race/ethnicity			.081
White, non-Hispanic	8638 (93.3)	625 (6.7)	
White, Hispanic	489 (91.2)	47 (8.8)	
Black	652 (91.8)	58 (8.2)	
Other or unknown race/ethnicity	344 (91.3)	33 (8.8)	
Marital status			.826
Married	9480 (93)	713 (7)	
Not married	643 (92.8)	50 (7.2)	
U.S. Census region			.207
Northeast	2037 (92.7)	160 (7.3)	
South	1221 (92.9)	94 (7.2)	
Midwest	2744 (93.8)	180 (6.2)	
West	4121 (92.6)	329 (7.4)	
Median census tract income, $†			.521
<35,000	2125 (93.1)	157 (6.9)	
35,000–44,999	2458 (93.6)	169 (6.4)	
45,000–59,999	2689 (93)	202 (7)	
≥60,000	2732 (92.6)	220 (7.4)	
Residents in census tract with less than high school education, %‡			.106
>25	2441 (92.9)	186 (7.1)	
15.1–25	2729 (93.3)	195 (6.7)	
10–15	2420 (93.6)	164 (6.4)	
<10	2494 (92)	216 (8)	
Tumor size, cm			<.001
≤4	3981 (87.5)	586 (12.5)	
>4	5543 (97.4)	146 (2.6)	
Unknown	599 (92.4)	49 (7.6)	
Tumor stage§			<.001
Localized	6757 (90.7)	692 (9.3)	
Regional	3368 (97.9)	71 (2.1)	
Tumor grade			<.001
Well differentiated	1151 (89.7)	132 (10.3)	
Moderately differentiated	3114 (92.7)	245 (7.3)	
Poorly or undifferentiated	2398 (96.2)	94 (3.8)	
Unknown	3460 (92.2)	292 (7.8)	
Charlson index score			.054
0	2090 (93.4)	360 (6.6)	
1	4155 (92.9)	319 (7.1)	
≥2	878 (91.3)	84 (8.7)	
Hypertension			<.001
Yes	4678 (92)	409 (8)	
No	5445 (93.9)	354 (6.1)	
Urolithiasis			.472
Yes	398 (92.1)	34 (7.9)	
No	9725 (93)	729 (7)	

(*continued*)

TABLE 1
(***continued***)

	No. of patients (%)		
Characteristic	Radical nephrectomy	Partial nephrectomy	P*
Renovascular disease			.813
Yes	157 (93.5)	11 (6.5)	
No	9966 (93)	752 (7)	

* Student *t* tests were used to compare the mean age between treatment groups, and chi-square tests were used for categorical variables.

† There were 389 patients who had information missing for income.

‡ There were 389 patients who had data missing for education.

§ Tumor stage data reported by the Surveillance, Epidemiology, and End results (SEER) Program represents a "best" staging system, which incorporates data from both pathologic and clinical staging. In the current study of patients who underwent surgery, nearly uniform application of pathologic staging was anticipated. For kidney cancers diagnosed between 1991 and 2001, American Joint Committee on Cancer staging classification was not available in the SEER registry; consequently, the categories for the tumor stage variable necessarily were limited to localized and regional disease.

DISCUSSION

Our principal findings clarify the benefits of nephron-sparing surgery for patients with early-stage kidney cancer. Among Medicare recipients who were diagnosed with kidney cancer between 2000 and 2002, partial nephrectomy was associated with a 26% lower risk of developing at least 1 adverse renal outcome; including a trend toward less frequent receipt of dialysis services, dialysis access surgery, or renal transplantation. The validity of our findings is strengthened by the use of propensity score techniques to balance the treatment cohorts on age, tumor size, and a broad range of prevalent comorbidities that influenced both the treatment received and the likelihood of adverse renal outcomes.[28,29] The consequent inference from these data are that partial nephrectomy is associated with less clinically apparent renal morbidity than radical nephrectomy.

We observed no association between surgery type and adverse renal outcomes among patients who were treated from 1991 to 1999. The discrepancy between treatment eras is consistent with our hypothesis that elective partial nephrectomy rarely was performed before 2000. Instead, nephron-sparing surgery was applied mainly among patients with indications like a solitary kidney, pre-existing chronic kidney disease, and/or comorbidities that threaten future renal function.[2,31] In 2000 and thereafter, conversely, most partial nephrectomies appear to have been performed electively. Accordingly, data from these contemporary patients more accurately reflect the potential benefits of nephron-sparing surgery

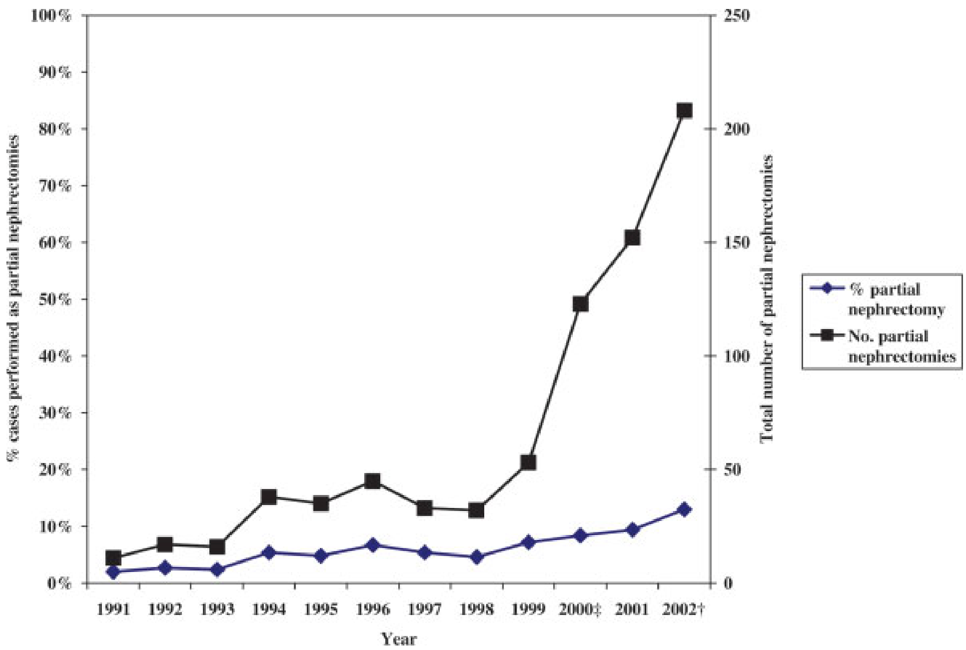

FIGURE 1. The annual number and proportion of partial nephrectomies from 1991 to 2002 ($P < .001$ for temporal trend). The double dagger indicates that 4 additional tumor registries began contributing cases to the linked Surveillance, Epidemiology, and End Results-Medicare dataset in 2000; single dagger, 16 partial nephrectomies were included among patients who were diagnosed in late 2002 but who did not undergo surgery until 2003.

among patients with a solitary renal mass and a normal contralateral kidney.

For this group of patients, preservation of nephrons in the tumor-bearing kidney appears to reduce the frequency of subsequent chronic kidney disease, postoperative nephrology consultations, physician services related to ESRD, and/or dialysis or transplantation services. Chronic kidney disease is associated with excess morbidity,[16] premature mortality,[16,17] and reduced health-related quality of life[17,32]; and dialysis is associated with even greater decrements in quality of life[32–34] and survival.[35,36] Hence, these data suggest that expanded use of nephron-sparing surgery could improve long-term health outcomes among patients who are treated for early-stage kidney cancer. Moreover, because annual hemodialysis expenditures exceed $70,000 for Medicare beneficiaries,[37] our findings also highlight potentially advantageous economic outcomes of partial nephrectomy.

That we demonstrated a disparity in adverse clinical events during an average follow-up of only 2 years is consistent with recent data describing a higher than previously recognized prevalence of chronic kidney disease[38] and occult glomerular pathology[39] among older Americans (ie, aged $\geq$60 years). Likewise, these data prompt speculation of even greater potential benefits from nephron-sparing surgery in younger kidney cancer patients who have a longer life expectancy (and who also may have a significant baseline prevalence of chronic kidney disease[38]).

We did not observe an association between treatment and postoperative cardiovascular morbidity. There are several plausible explanations for this finding, including insufficient follow-up to compare elective partial and radical nephrectomy (ie, patients in the later treatment era), residual confounding by unmeasured cardiovascular risk factors, or simply that differential preservation of renal function after partial versus radical nephrectomy is a relatively small determinant of cardiovascular disease risk among this cohort of elderly patients (many of whom have multiple concurrent risk factors).

Taken together, these data indicate that, on average, elective partial nephrectomy is associated with less clinically apparent renal morbidity than radical nephrectomy. Because cancer control appears to be equivalent for tumors that measure up to 4 cm (and perhaps even 7 cm),[3–6,18,40] the observed reduction in renal morbidity motivates expanded use of elective partial nephrectomy among patients with small renal masses. This conclusion is tempered, however, by the limitations of our study design. In

TABLE 2
Distribution of Covariates by Propensity Score Strata According to Receipt of Partial Nephrectomy

Type of nephrectomy	Propensity score strata (Range)*									
	Stratum 1 (0.003–0.01)[†]	Stratum 2 (0.01–0.02)	Stratum 3 (0.02–0.03)	Stratum 4 (0.03–0.034)	Stratum 5 (0.034–0.04)	Stratum 6 (0.04–0.06)	Stratum 7 (0.06–0.10)	Stratum 8 (0.10–0.13)	Stratum 9 (0.13–0.16)	Stratum 10 (0.16–0.32)[‡]
No. of patients	1088	1089	1089	1088	1089	1089	1088	1089	1089	1088
Partial	9	20	21	36	32	43	93	132	153	224
Radical	1079	1069	1068	1052	1057	1046	995	957	936	864
Mean age [SD], y										
Partial	78.6 [6.3]	73.9 [5.3]	77.5 [5]	75.6 [5]	74.4 [5.8]	72.8 [5.1]	75.4 [5.6]	76.2 [4.4]	73.1 [4.6]	70.1 [3.9]
Radical	77.5 [6.2]	73.4 [5.8]	77.5 [6.4]	76 [5.6]	73.4 [5.2]	71.7 [5]	76.0 [7]	75.8 [5.1]	73.2 [5]	70.4 [4.2]
White, %										
Partial	77.8	75	85.7	86.2	87.5	83.7	80.7	94.7	84.3	71.9
Radical	93.8	81.3	88.5	92.3	84.8	78.4	82.3	91.9	88.6	68.9
Married, %										
Partial	88.9	90	95.2	91.7	93.8	90.7	91.4	97	94.8	92.4
Radical	94.6	93.4	94	94.1	93.6	92.8	93.2	94.6	94.2	91.8
Highest income quartile, %										
Partial	22.2	25	23.8	19.4	15.6	44.2	17.2	24.2	26.1	26.3
Radical	20.2	24.5	18.8	22.8	26	27	21.9	23.5	25	25.2
Highest education quartile, %										
Partial	11.1	30	23.8	30.6	15.6	48.8	24.7	23.5	27.5	31.7
Radical	24.7	23.3	20.5	24	27.3	27.7	22.2	24	27.2	25.6
Northeast Census region, %										
Partial	33.3	25	14.3	11.1	28.1	25.6	16.1	20.5	28.8	17.4
Radical	15.8	20	18.5	20.6	21.4	20.1	19.8	23.2	23.4	19
Tumor size $\leq$4 cm, %										
Partial	0	0	0	11.1	18.8	37.2	64.5	89.4	95.4	97.3
Radical	0	0.6	8.2	16.3	17	26	68	89.3	93.7	98.9
Localized tumor stage, %										
Partial	0	15.8	87	84.9	80.6	59.5	82.3	100	100	100
Radical	0	4.9	63.3	77.2	77.9	71.8	83.3	99.9	100	100
Well or moderately differentiated tumor grade, %										
Partial	11.1	40	19	33.3	59.4	39.5	46.2	53	53.6	54
Radical	24.1	34.7	36.6	38.8	44	45	45.5	51.7	50.6	55.2
Charlson index score <2, %										
Partial	77.8	75	100	96.8	87.5	90.7	91.4	96.2	93.5	82.1
Radical	95.2	91.9	94	94.2	91.2	87.8	90.5	93.2	91	82.4
Hypertension, %										
Partial	33.3	50	28.6	36.1	65.6	69.8	34.4	31.1	50.3	78.6
Radical	25.3	54.5	30.2	37.6	50.1	68.7	40.9	33.3	49.5	77.1

(*continued*)

TABLE 2
(*continued*)

Type of nephrectomy	Propensity score strata (Range)*									
	Stratum 1 (0.003–0.01)†	Stratum 2 (0.01–0.02)	Stratum 3 (0.02–0.03)	Stratum 4 (0.03–0.034)	Stratum 5 (0.034–0.04)	Stratum 6 (0.04–0.06)	Stratum 7 (0.06–0.10)	Stratum 8 (0.10–0.13)	Stratum 9 (0.13–0.16)	Stratum 10 (0.16–0.32)‡
Urolithiasis, %										
Partial	0	0	0	2.8	3.1	7	4.3	3	5.9	5.4
Radical	3.2	3.4	3.9	3.1	3.5	5.4	4.1	4	3.1	6
Renovascular disease %										
Partial	11.1	0	0	0	3.1	4.7	0	0	2	1.8
Radical	2.7	2.7	1	0.7	1.2	1.4	2.3	0.4	0.8	2.2

* For presentation, propensity scores were rounded to 2 decimal places; there was no overlap in propensity scores between strata. The distribution of each covariate was similar within each propensity score strata (all $P > .05$).
† Patients in this stratum had the lowest propensity for receiving partial nephrectomy.
‡ Patients in this stratum had the highest propensity for receiving partial nephrectomy.

TABLE 3
Adverse Renal and Cardiovascular Outcomes After Partial Versus Radical Nephrectomy Stratified by Treatment Era

Outcome*	Treatment years 1991–1999, n = 5981				Treatment years 2000–2002, n = 4905			
	% Partial nephrectomy, n = 280†	% Radical nephrectomy, n = 5701‡	Adjusted HR (95% CI)§	*P*	% Partial nephrectomy, n = 483†	% Radical nephrectomy, n = 4422‡	Adjusted HR (95% CI)§	*P*
Any adverse renal outcome	33.9	27.4	1.18 (0.96–1.46)	0.124	16.4	21.8	0.74 (0.58–0.94)	.012
Dialysis or transplantation	11.4	6.2	1.26 (0.86–1.84)	0.241	2.7	4.7	0.58 (0.33–1.04)	.066
Any adverse cardiovascular outcome	72.1	67.3	1.02 (0.88–1.18)	0.768	51.1	50.8	1.02 (0.92–1.22)	.403

HR indicates hazard ratio; 95% CI, 95% confidence interval.
* Patients were censored if they did not meet criteria for an adverse renal or cardiovascular outcome either on December 31, 2003 (last date for available Medicare claims) or on their date of death (if they died prior to the end of the study interval).
† The median follow-up for the partial nephrectomy cohort was 60.5 months for treatment years 1991–1999 and 23.7 months for treatment years 2000–2002.
‡ The median follow-up for the radical nephrectomy cohort was 59.3 months for treatment years 1991–1999 and 23.1 months for treatment years 2000–2002.
§ Adjusted for propensity score strata, age, race/ethnicity, U.S. Census region, education, income, tumor size, tumor stage, tumor grade, and pre-existing comorbidity (Charlson index score, hypertension, urolithiasis, and renovascular disease). Radical nephrectomy was the reference group.

particular, propensity scores do not eliminate bias due to unmeasured differences between treatment groups.[28,29] This limitation may be most relevant to our observation that partial nephrectomy is associated with improved overall survival among patients who were treated from 2000 through 2002. If, during this treatment era, lower risk patients—as defined by performance status, frailty, or other unmeasured variables—were selected preferentially for elective partial nephrectomy, then the survival differences reported herein likely reflect residual selection bias rather than a protective effect of partial nephrectomy. Ultimately, this finding will be confirmed or refuted by the results of an European Organization for Research and Treatment of Cancer (EORTC)-led randomized controlled trial comparing mortality outcomes after elective partial or radical nephrectomy.[15]

Conversely, given our ability to measure and adjust for prevalent renal insufficiency and comorbidities that threaten long-term renal function, selection bias is less likely to fully explain the reduction in renal morbidity associated with partial nephrectomy. Although the EORTC trial compares acute surgical side-effects,[15] it was not designed to assess longer term renal (or cardiovascular) morbidity after partial or radical nephrectomy. In the absence of such randomized data, our preliminary findings may encourage the establishment of a prospective, national registry that collects detailed baseline clinical data and subsequently compares specific nononcologic health outcomes after radical or partial nephrectomy.

It is also important to recognize that the outcomes we measured are not the only factors that influence the choice between partial and radical nephrectomy. Partial nephrectomy is not always feasible technically; moreover, its safe application may be limited by availability of adjuvant services (eg, interventional radiology, intraoperative ultrasound) that are necessary to ensure optimal perioperative care. Furthermore, some patients may prefer a straightforward radical nephrectomy (which more often can be performed laparoscopically), given the potential for a more complicated short-term recovery after partial nephrectomy.[15] Treatment decisions, appropriately, are based in part on a patient's preferences for the potentially dissimilar outcomes (eg, risk of ipsilateral tumor recurrence, procedure-related complications, intensity of convalescence) after the 2 procedures.

Our study has several additional limitations. First, its generalizability is restricted, because our sample included only patients who were aged ≥66 years and who had traditional fee-for-service Medicare. Nonetheless, linked SEER-Medicare data provide a unique opportunity to evaluate treatment outcomes in the context of clinically important casemix variables, including tumor size and medical comorbidity. Second, our findings are based on an administrative claims dataset, the reliability of which is limited by the accuracy of coding practices. In particular, underreporting and misclassification of outcomes are possible in the current analysis; however, if present, both types of measurement bias should occur uniformly across treatment groups. Third, although we posit that expanded the use of partial nephrectomy is a desirable objective among select patients with kidney cancer, we also recognize that clarifying its optimal use will require a better understanding of patient preferences.[41] Finally, we could not explicitly measure all clinical variables that influence the decision between partial or radical nephrectomy, including tumor location, family history and/or hereditary kidney cancer syndromes, and symptoms at presentation.

Among the patients with kidney cancer who were diagnosed in or after 2000, partial nephrectomy was associated with a reduced risk of adverse renal health outcomes, including less frequent receipt of dialysis or transplantation-related services. These data substantiate the clinical benefits of nephron-sparing surgery among patients with early-stage kidney cancer. Nonetheless, given the potential for selection bias and residual confounding in this observational cohort, prospective studies are necessary to confirm our findings.

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