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The association between chronic renal failure and renal cell carcinoma may differ between black and white Americans

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Abstract

Purpose—In the United States, renal cell carcinoma (RCC) incidence is higher among blacks than among whites. Risk of RCC is elevated among end-stage renal disease patients, although no studies have looked at differences by race in the relationship between chronic renal failure and RCC.

Methods—We investigated RCC risk in relation to chronic renal failure in a population-based case-control study of blacks and whites in Chicago and Detroit. Data, including information on kidney disease, were collected from interviews with 1,217 RCC cases (361 blacks, 856 whites) and 1,235 controls (523 blacks, 712 whites). Odds ratios (OR) and 95% confidence intervals (CI) were estimated using unconditional logistic regression.

Results—Risk of RCC was increased in relation to chronic renal failure (OR 4.7, 95% CI 2.2–10.1) and dialysis (OR 18.0, 95% CI 3.6–91). The association remained after defining exposure as those who had chronic renal failure ≥10 years prior to RCC diagnosis. Chronic renal failure was more strongly associated with RCC among blacks than among whites (OR 8.7, 95% CI 3.3–22.9 and 2.0, 0.7–5.6 respectively; $P_{interaction}$=0.03) and among those without a history of diabetes relative to diabetic subjects (OR 8.3, 95% CI 3.1–22.7 and 1.9, 0.6–5.9 respectively; $P_{interaction}$=0.03).

Conclusions—These results suggest that chronic renal failure is a strong risk factor for RCC, particularly among black and non-diabetic subjects. Our findings of differences in risk estimates by race, to our knowledge the first such report, require replication.

Keywords

renal cell carcinoma; kidney cancer; chronic renal failure; end-stage renal disease; racial disparities

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Introduction

The incidence of renal cell carcinoma (RCC) is higher among blacks than among whites in the United States (US), and incidence rates have risen more rapidly among blacks than among whites in recent decades [1]. Based on data from the US Surveillance, Epidemiology, and End Results (SEER) program for the years 2002–2005, the age-adjusted RCC incidence rates among black men, white men, black women, and white women were 17.0, 14.3, 7.5 and 7.2 per 100,000 person-years, respectively [2].

Previous studies have consistently observed an increased risk of RCC among patients with end-stage renal disease (ESRD) and kidney transplant recipients [3–7]. In the US, the incidence of ESRD is considerably higher among blacks than among whites; in 2009, the rates for initiating hemodialysis were 928.3 and 251.0 per million population among blacks and whites, respectively [8]. Diabetes is the leading cause of ESRD both overall and among blacks; however, the incidence of hypertension-related ESRD is particularly high among blacks relative to any other racial or ethnic group [9]. Despite these racial disparities in the incidence of both ESRD and RCC, to our knowledge, no previous studies of chronic renal failure and RCC risk have evaluated differences by race. To address this research gap, we conducted an analysis of RCC risk in relation to chronic renal failure in a population-based case-control study of blacks and whites in the US.

Materials and Methods

Study population

This population-based case-control study was conducted in two metropolitan regions in the US: Detroit, Michigan and Chicago, Illinois. Methods for subject recruitment and data collection have been described [10]. Briefly, whites and blacks between 20 and 79 years of age who were newly diagnosed with histologically confirmed RCC (ICD-O-3 C64.9) between 2002 and 2007 were eligible to participate as cases. Patients with RCC in a transplanted kidney were deemed ineligible and excluded. Cases in Detroit were identified through the Metropolitan Detroit Cancer Surveillance System (a SEER registry), and cases in Chicago were identified by reviewing pathology reports at hospitals in Cook County. To increase enrollment of blacks in this study, all eligible cases who were black were invited to participate, whereas only a subset of potentially eligible cases who were white (selected based on age- and sex-specific strata) were recruited.

Controls were selected from the general population and were frequency matched to cases on age, sex, race, and metropolitan area of residence. Controls between 65 and 79 years of age were identified from Medicare eligibility files, and controls under age 65 were identified from department of motor vehicle (DMV) records. Our targeted matching frequency of controls to cases was 2:1 for blacks and 1:1 for whites. Because information on race was unavailable in the DMV records but addresses were available, we oversampled people in Census block groups with a high proportion of black residents to help achieve the targeted matching ratios for blacks under age 65.

We identified 1,918 eligible cases for this study, of whom 171 died before they could be contacted or interviewed, 92 could not be located, and 21 moved out of the study areas. Physicians declined to give permission to contact 63 cases, leaving 1,571 eligible cases who we attempted to recruit. Among these cases, 221 declined to participate and 133 were not interviewed due to serious illness, impairment, or nonresponse after multiple contact attempts. In total, 1,217 RCC cases (361 blacks and 856 whites) were enrolled in this study (78% of the cases that we attempted to recruit overall; 79% and 78% of blacks and whites with known race, respectively). Of the 2,718 presumed eligible controls that we identified,

41 died before they could be contacted or interviewed, 345 could not be located, and 63 moved out of the study areas, leaving 2,269 eligible controls who we attempted to recruit. Among these controls, 677 declined to participate and 357 were not interviewed due to serious illness, impairment, or nonresponse after multiple contact attempts. We enrolled 1,235 controls in this study (54% of the eligible controls that we attempted to recruit). For controls identified through Medicare eligibility files (65–79 years of age), the response proportion was 53% overall (50% and 55% of blacks and whites, respectively). For controls identified through DMV records (<65 years of age), the response proportion was 55% overall. As noted above, information on race was unavailable in DMV records. However, based on our classification of Census block groups by the proportion of residents who were black, the response proportion was 59% in areas with a high density of black residents and 52% in areas with a low density of black residents. Study procedures were approved by Institutional Review Boards at collaborating institutions, and written informed consent was obtained from all subjects.

Characterization of chronic renal failure and other covariates

History of chronic renal failure and other medical conditions (e.g., hypertension, diabetes) was determined from in-depth computer-assisted personal interviews that were conducted by trained interviewers in participants' homes. We asked participants to report medical conditions that were diagnosed by a health professional at least two years before the date of the interview. For each reported condition, the participant was asked to provide age or year of diagnosis. Participants were also asked to report treatments received, including dialysis and kidney transplantation. Information on demographic characteristics, height, weight, smoking history, family history of cancer, and other covariates was also collected in the interviews.

Statistical analysis

Risk of RCC was assessed in relation to history of chronic renal failure and ESRD necessitating dialysis and/or kidney transplantation. To assess RCC risk based on severity of kidney disease and ESRD management, analyses were also performed separately for subjects considered to have ESRD (dialysis and transplant recipients) and for subjects reporting chronic renal failure but not dialysis or kidney transplantation. Odds ratios (OR) and 95% confidence intervals (CI) were estimated using unconditional logistic regression. Analyses were performed with adjustment for matching factors [sex, age (<45y, 45–54y, 55–64y, 65–74y, ≥75y), race (white, black) and study center] and also further adjusted for level of education (<12y, high school graduate, some college, college graduate), smoking status (never, occasional, regular former, regular current), body mass index (BMI; <25, 25–29.9, 30–34.9, ≥35), history of hypertension (no, yes), and family history of cancer (none, kidney cancer, any other cancer). The results reported in the text are based on the fully adjusted models unless otherwise noted. Analyses were also repeated after adjusting for level of blood pressure control among hypertensive individuals. As described in detail in Colt et al. [10], sample weights were applied to address potential bias due to differential sampling rates among cases and controls, differential participation rates between cases and controls, survey nonresponse, and deficiencies in coverage of the population at risk in control selection. The sample weights for controls also included a post-stratification adjustment to ensure that the weighted distributions across matching variables were the same for cases and controls. All logistic regression analyses incorporated sample weights. Standard errors were estimated using Jackknife replicate weights [11]. If odds ratios could not be defined because none of the controls had a history of dialysis or kidney transplantation, we performed chi-squared tests adjusted for sample weights. In these analyses, Fisher's exact tests were also performed on unweighted data because this method is accurate for small sample sizes.

We evaluated RCC risk in relation to chronic renal failure after stratifying by race, sex, age at RCC diagnosis (20–64 years, 65–79 years), time after diagnosis of chronic renal failure (<10 years, ≥10 years prior to reference date), and history of diabetes. Analyses stratified by history of hypertension were not performed because very few cases with chronic renal failure did not have hypertension (N=4). Tests of multiplicative interaction were performed using the Wald test for the joint significance of additional cross-product terms in the logistic regression model. Polytomous logistic regression models were used to evaluate RCC risk by tumor subtype classified by central pathology review and morphology codes from medical records [clear cell adenocarcinoma (ICD-O-3 morphology code 8310), papillary adenocarcinoma (ICD-O-3 morphology code 8260)], tumor stage at diagnosis (localized, regional/distant), and tumor grade (grade 1, grade 2, grades 3/4). Because 84% of all subjects were enrolled through the Detroit study center and cases in Detroit were identified from the SEER registry, sensitivity analyses restricted to subjects from Detroit were also performed. All statistical analyses were performed using Stata version 10.1 (StataCorp LP, College Station, TX). Findings were considered statistically significant if two-sided *P*-values were <0.05.

Results

Cases (N=1,217) were more likely than controls (N=1,235) to be obese (BMI ≥ 30), to smoke, and to have a history of hypertension (Table 1). We observed a statistically significant increased risk of RCC in relation to history of chronic renal failure (fully adjusted OR 4.7, 95% CI 2.2–10.1; Table 2). Risk of RCC was significantly higher among subjects with ESRD who received dialysis (OR 18.0, 95% CI 3.6–91) or a transplanted kidney (15 cases, 0 controls; $P<0.001$, chi-squared test and unweighted Fisher's exact test). To further evaluate RCC risk in relation to kidney disease severity and ESRD management, we analyzed chronic renal failure, dialysis, and kidney transplantation in combination with one another. Subjects who reported a history of chronic renal failure without dialysis or kidney transplantation had a higher risk of RCC than those without chronic renal failure, although this association was not statistically significant (16 cases, 9 controls, OR 1.8, 95% CI 0.7–4.3). History of ESRD managed only with dialysis, but not kidney transplantation, was associated with a statistically significant increased risk of RCC (21 cases, 3 controls, OR 10.3, 95% CI 1.9–56). Almost all subjects with ESRD who received a transplanted kidney had also been on dialysis (14 cases, 0 controls); risk of RCC was significantly elevated among these individuals ($P<0.001$, chi-squared test and unweighted Fisher's exact test).

The association between chronic renal failure and RCC was considerably stronger among blacks than among whites (OR 8.7, 95% CI 3.3–22.9 and 2.0, 0.7–5.6 respectively; $P_{int}=0.03$; Table 3). After restricting to subjects with a history of chronic renal failure but not dialysis or kidney transplantation, we observed an increased risk among blacks (10 cases, 4 controls, OR 4.1, 95% CI 1.2–13.7) but not among whites (6 cases, 5 controls, OR 1.0, 95% CI 0.3–3.5). We also found that chronic renal failure was more strongly associated with RCC risk among subjects who did not report a history of diabetes relative to those with diabetes (OR 8.3, 95% CI 3.1–22.7 and 1.9, 0.6–5.9 respectively; $P_{int}=0.03$). We followed up on this finding by performing an analysis restricted to subjects with a history of hypertension but not diabetes. Within this subgroup, the difference in history of chronic renal failure between cases and controls was particularly great; 30 cases (5.6%) had a history of chronic renal failure, whereas none of the controls had a history of chronic renal failure ($P<0.001$, chi-squared test and Fisher's exact test).

Stronger associations were observed among subjects who were diagnosed with chronic renal failure 10 or more years prior to RCC diagnosis and among subjects diagnosed with RCC

before age 65, although differences in risk estimates were not statistically significant for either time after diagnosis of chronic renal failure (P_{int}=0.79) or age at RCC diagnosis (P_{int}=0.35; Table 3). We did not observe any notable difference by sex in the association between chronic renal failure and RCC risk (P_{int}=0.94).

When we further adjusted for level of control of hypertension, our results for chronic renal failure were essentially unchanged (OR 4.5, 95% CI 2.1–9.6). No differences in the relationship between chronic renal failure and RCC risk were observed by histologic subtype, stage, or grade (not shown). Results of the main analyses were essentially unchanged after restricting to subjects from Detroit only (e.g., chronic renal failure: OR 4.5, 95% CI 1.9–10.4).

Discussion

The results from this population-based case-control study provide further evidence that chronic renal failure is an important risk factor for RCC development, and suggest that the association is particularly strong among patients who are black, have non-diabetic chronic renal failure, or have had chronic renal failure for an extended time period (≥10 years). To our knowledge, this is the first report of a stronger association between chronic renal failure and RCC risk among blacks than among whites. The reason for the stronger association between chronic renal failure and risk of RCC observed among blacks relative to the association observed among whites is unclear. It may be due to racial differences in: the prevalence of hypertension-related ESRD [9, 12], which may be more strongly associated with RCC than diabetes-related ESRD [4, 5]; access to care or aggressiveness of treatment for chronic renal failure [13, 14]; modifiable risk factors related to both chronic renal failure and RCC (e.g., obesity, smoking) [15]; and/or genetic susceptibility [16–18]. Several recent reports identified genetic variants in *APOL1* that are associated with an increased risk of hypertension-related ESRD, focal segmental glomerulosclerosis, and HIV-associated nephropathy among African Americans [16–18]. The *APOL1* risk alleles are found exclusively among individuals of African descent and may explain in part the excess of nondiabetic chronic kidney disease among African Americans. Whether variants in *APOL1* or other genetic variants associated with hypertension-related ESRD (e.g., *MTHFR*; ref [19]) contribute to the excess risk of RCC among blacks is as yet unknown.

Various biologic mechanisms underlying the association between chronic renal failure and RCC have been proposed. Pathologic changes in the kidney related to loss of renal function (e.g., renal fibrosis, tubular atrophy, interstitial inflammation, and acquired cystic kidney disease) may lead to RCC development [5], although it has been suggested that impairment of immunity in ESRD and kidney transplantation may also play a role [6]. We observed stronger associations with increasing severity of kidney disease, as determined by history of dialysis and kidney transplantation. These findings suggest that risk of RCC may increase along a continuum from underlying medical conditions – hypertension in particular – that lead to chronic renal failure and ultimately require renal replacement therapy. As noted by Stewart et al. [6], there is little evidence that dialysis itself is responsible for the increased risk of RCC among patients receiving this treatment. Rather, the strong association between dialysis and RCC risk is likely due to pathologic changes related to loss of renal function; complications of chronic renal failure include development of acquired cystic kidney disease, which is more prevalent among dialysis patients and is a known risk factor for RCC [5, 20]. We observed a particularly strong association between kidney transplantation and risk of RCC in a native kidney (cases of RCC in non-native kidneys were excluded from this study). This association is also likely to be attributable to pathologic changes in the kidney related to ESRD, although some immunosuppressive medications administered to prevent

rejection of the transplanted kidney could potentially contribute to the excess risk of RCC [21, 22].

Previous studies have reported an increased risk of RCC among individuals with ESRD who are on dialysis and among patients who have undergone kidney transplantation [3–7]. These studies have consistently observed stronger associations between chronic renal failure and RCC with increasing time on dialysis, and also among younger individuals. Two studies evaluated the relationship between ESRD and RCC after stratifying by primary renal disease [4, 5]; both studies reported weaker associations for ESRD due to diabetes than for ESRD related to hypertension or other renal diseases. Consistent with these previous reports, we observed a weaker association between chronic renal failure and RCC risk among subjects with a history of diabetes relative to non-diabetic subjects. We also found that the association between chronic renal failure and RCC was stronger among subjects who had chronic renal failure for ≥10 years or were under age 65 at the time of RCC diagnosis. The consistency of our findings with previous reports lends credence to the validity of these data.

With 1,217 cases and 1,235 controls, this study is, to our knowledge, the largest case-control study to evaluate risk of RCC in relation to chronic renal failure. Moreover, the relatively large number of black subjects enrolled in this study allowed us to investigate how the relation between chronic renal failure and RCC risk differs by race, which has not been evaluated in previous studies [15]. Although many previous registry-based investigations have evaluated the relation between ESRD and RCC risk, these studies often lack information on modifiable risk factors for RCC such as smoking status, obesity, and hypertension. We were able to adjust for these factors in multivariate models, thus reducing the potential for confounding.

This study also had limitations. Despite the large number of black and white subjects in this study, because chronic renal failure is a rare condition in the general population we had limited statistical power for analyses stratified by race and for tests of interaction; as such, our confidence intervals for race-specific risk estimates were fairly wide. History of chronic renal failure was based on self-report by participants during a structured interview and may be subject to misclassification. Because we did not have information on the estimated glomerular filtration rate for study participants, we were unable to confirm diagnoses of chronic renal failure or classify chronic kidney disease by stage. However, the sample-weighted prevalence of chronic renal failure among controls in our study was 1.2% for blacks and 0.7% for whites, which is consistent with evidence of a higher prevalence of measurement-based stage 4/5 chronic kidney disease for blacks (1.1%) than for whites (0.3%) among U.S. adults participating in the National Health and Nutrition Examination Survey (NHANES) between 1999 and 2004 [23]. The consistency between our estimates of prevalence of chronic renal failure among black and white controls and measurement-based prevalence estimates in NHANES suggests that the self-reported excess of chronic renal failure among blacks in our study is real and likely has contributed to the black excess in RCC.

Because our observed association between chronic renal failure and RCC risk was largely confined to individuals with a history of hypertension, the potential for residual confounding by hypertension in our study was a concern. However, the association between chronic renal failure and RCC remained after adjusting for history of hypertension, and risk estimates were essentially unchanged when we adjusted for degree of blood pressure control. Furthermore, the association that we observed for chronic renal failure was stronger than the association reported previously for hypertension [10]; as such, residual confounding by hypertension cannot plausibly explain our findings.

It is possible that heightened clinical surveillance among individuals with chronic renal failure could lead to falsely high ORs due to detection bias. However, our findings for the association between chronic renal failure and RCC were similar after stratifying by tumor stage at diagnosis. Since we would expect detection bias to be more of a concern for localized tumors than for tumors with regional or distant metastases, the fact that we did not see material differences by tumor stage suggests that the impact of heightened surveillance on our findings was likely minimal. Nonetheless, replication in other populations with greater uniformity of screening practices (e.g., HMO participants) is needed to confirm these findings.

In conclusion, the findings from this study suggest that chronic renal failure is a strong risk factor for RCC development, particularly among blacks and among individuals without a history of diabetes. This study is, to our knowledge, the first to report differences in RCC risk in relation to history of chronic renal failure between blacks and whites; these findings need to be confirmed in other population- and registry-based studies.

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References

1. Chow WH, Dong LM, Devesa SS. Epidemiology and risk factors for kidney cancer. Nat Rev Urol. 2010; 7:245–57. [PubMed: 20448658]
2. Chow WH, Devesa SS. Contemporary epidemiology of renal cell cancer. Cancer J. 2008; 14:288–301. [PubMed: 18836333]
3. Engels EA, Pfeiffer RM, Fraumeni JF, Kasiske BL, Israni AK, Snyder JJ, RAW, Goodrich NP, Bayakly AR, Clarke CA, Copeland G, Finch JL, et al. Spectrum of cancer risk among US solid organ transplant recipients. JAMA. 2011; 306:1891–901. [PubMed: 22045767]
4. Maisonneuve P, Agodoa L, Gellert R, Stewart JH, Buccianti G, Lowenfels AB, Wolfe RA, Jones E, Disney AP, Briggs D, McCredie M, Boyle P. Cancer in patients on dialysis for end-stage renal disease: an international collaborative study. Lancet. 1999; 354:93–9. [PubMed: 10408483]
5. Stewart JH, Buccianti G, Agodoa L, Gellert R, McCredie MR, Lowenfels AB, Disney AP, Wolfe RA, Boyle P, Maisonneuve P. Cancers of the kidney and urinary tract in patients on dialysis for end-stage renal disease: analysis of data from the United States, Europe, and Australia and New Zealand. J Am Soc Nephrol. 2003; 14:197–207. [PubMed: 12506152]
6. Stewart JH, Vajdic CM, van Leeuwen MT, Amin J, Webster AC, Chapman JR, McDonald SP, Grulich AE, McCredie MR. The pattern of excess cancer in dialysis and transplantation. Nephrol Dial Transplant. 2009; 24:3225–31. [PubMed: 19589786]
7. Vajdic CM, McDonald SP, McCredie MR, van Leeuwen MT, Stewart JH, Law M, Chapman JR, Webster AC, Kaldor JM, Grulich AE. Cancer incidence before and after kidney transplantation. JAMA. 2006; 296:2823–31. [PubMed: 17179459]
8. United States Renal Data System. USRDS 2011 Annual Data Report: Atlas of Chronic Kidney Disease and End-Stage Renal Disease in the United States. Bethesda, MD: National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases; 2011.
9. Martins D, Tareen N, Norris KC. The epidemiology of end-stage renal disease among African Americans. Am J Med Sci. 2002; 323:65–71. [PubMed: 11863081]

10. Colt JS, Schwartz K, Graubard BI, Davis F, Ruterbusch J, Digaetano R, Purdue M, Rothman N, Wacholder S, Chow WH. Hypertension and Risk of Renal Cell Carcinoma Among White and Black Americans. Epidemiology. 2011; 22:797–804. [PubMed: 21881515]
11. Rust KF, Rao JN. Variance estimation for complex surveys using replication techniques. Stat Methods Med Res. 1996; 5:283–310. [PubMed: 8931197]
12. McClellan W, Tuttle E, Issa A. Racial differences in the incidence of hypertensive end-stage renal disease (ESRD) are not entirely explained by differences in the prevalence of hypertension. Am J Kidney Dis. 1988; 12:285–90. [PubMed: 3263042]
13. Klein JB, Nguyen CT, Saffore L, Modlin C 3rd, Modlin CS Jr . Racial disparities in urologic health care. J Natl Med Assoc. 2010; 102:108–17. [PubMed: 20191923]
14. Weng FL, Joffe MM, Feldman HI, Mange KC. Rates of completion of the medical evaluation for renal transplantation. Am J Kidney Dis. 2005; 46:734–45. [PubMed: 16183429]
15. Lipworth L, Tarone RE, McLaughlin JK. Renal cell cancer among African Americans: an epidemiologic review. BMC Cancer. 2011; 11:133. [PubMed: 21486465]
16. Genovese G, Friedman DJ, Ross MD, Lecordier L, Uzureau P, Freedman BI, Bowden DW, Langefeld CD, Oleksyk TK, Uscinski Knob AL, Bernhardy AJ, Hicks PJ, et al. Association of trypanolytic ApoL1 variants with kidney disease in African Americans. Science. 2010; 329:841–5. [PubMed: 20647424]
17. Kopp JB, Nelson GW, Sampath K, Johnson RC, Genovese G, An P, Friedman D, Briggs W, Dart R, Korbet S, Mokrzycki MH, Kimmel PL, et al. APOL1 Genetic Variants in Focal Segmental Glomerulosclerosis and HIV-Associated Nephropathy. J Am Soc Nephrol. 2011; 22:2129–37. [PubMed: 21997394]
18. Papeta N, Kiryluk K, Patel A, Sterken R, Kacak N, Snyder HJ, Imus PH, Mhatre AN, Lawani AK, Julian BA, Wyatt RJ, Novak J, et al. APOL1 Variants Increase Risk for FSGS and HIVAN but Not IgA Nephropathy. J Am Soc Nephrol. 2011; 22:1991–6. [PubMed: 21997397]
19. Fung MM, Salem RM, Lipkowitz MS, Bhatnagar V, Pandey B, Schork NJ, O'Connor DT. Methylenetetrahydrofolate reductase (MTHFR) polymorphism A1298C (Glu429Ala) predicts decline in renal function over time in the African-American Study of Kidney Disease and Hypertension (AASK) Trial and Veterans Affairs Hypertension Cohort (VAHC). Nephrol Dial Transplant. 2011; 27:197–205. [PubMed: 21613384]
20. Heidland A, Bahner U, Vamvakas S. Incidence and spectrum of dialysis-associated cancer in three continents. Am J Kidney Dis. 2000; 35:347–51. discussion 52-3. [PubMed: 10676739]
21. Guba M, Graeb C, Jauch KW, Geissler EK. Pro- and anti-cancer effects of immunosuppressive agents used in organ transplantation. Transplantation. 2004; 77:1777–82. [PubMed: 15223891]
22. Gutierrez-Dalmau A, Campistol JM. Immunosuppressive therapy and malignancy in organ transplant recipients: a systematic review. Drugs. 2007; 67:1167–98. [PubMed: 17521218]
23. Prevalence of chronic kidney disease and associated risk factors--United States, 1999–2004. MMWR Morb Mortal Wkly Rep. 2007; 56:161–5. [PubMed: 17332726]

Table 1

Characteristics of cases and controls, overall and stratified by race[a]

	All participants		White participants		Black participants	
Characteristic	**Cases (N=1,217)**	**Controls (N=1,235)**	**Cases (N=856)**	**Controls (N=712)**	**Cases (N=361)**	**Controls (N=523)**
Sex						
Female	497 (38.2)	546 (38.6)	361 (38.0)	273 (38.4)	136 (38.8)	273 (39.2)
Male	720 (61.8)	689 (61.4)	495 (62.0)	439 (61.6)	225 (61.3)	250 (60.8)
Age at reference date (years)						
<45	147 (10.5)	179 (10.5)	106 (10.2)	93 (10.2)	41 (11.6)	86 (11.6)
45–54	287 (21.6)	270 (21.6)	185 (20.0)	145 (20.0)	102 (26.1)	125 (26.1)
55–64	372 (29.4)	350 (29.4)	255 (29.1)	205 (29.1)	117 (30.2)	145 (30.2)
65–74	303 (27.1)	329 (27.1)	221 (28.1)	196 (28.1)	82 (24.3)	133 (24.3)
75+	108 (11.5)	107 (11.5)	89 (12.7)	73 (12.7)	19 (7.9)	34 (7.9)
Study center						
Detroit	1,018 (83.3)	1,038 (82.7)	738 (84.9)	611 (83.9)	280 (78.6)	427 (79.0)
Chicago	199 (16.7)	197 (17.3)	118 (15.1)	101 (16.1)	81 (21.4)	96 (21.0)
Level of education						
<12 years	200 (16.7)	165 (12.0)	103 (12.7)	65 (9.4)	97 (28.1)	100 (19.1)
High school graduate	419 (34.5)	390 (31.5)	315 (36.6)	214 (30.8)	104 (28.7)	176 (33.5)
Some college	328 (26.3)	356 (27.3)	215 (24.9)	184 (25.6)	113 (30.3)	172 (32.1)
College graduate	270 (22.5)	324 (29.3)	223 (25.9)	249 (34.2)	47 (12.8)	75 (15.3)
Smoking status						
Never	432 (35.3)	471 (38.4)	309 (35.8)	287 (39.9)	123 (33.9)	184 (34.4)
Occasional	55 (4.7)	52 (3.8)	34 (4.2)	25 (3.5)	21 (6.2)	27 (4.9)
Regular former	410 (34.7)	445 (38.0)	304 (36.5)	276 (39.3)	106 (29.4)	169 (34.3)
Regular current	320 (25.3)	264 (19.7)	209 (23.5)	124 (17.4)	111 (30.5)	140 (26.4)
Missing	0	3	0	0	0	3
BMI (kg/m^2)[b]						
<25	240 (19.5)	366 (29.1)	172 (19.6)	216 (29.4)	68 (19.1)	150 (28.1)
25–29.9	436 (37.4)	493 (41.7)	310 (37.7)	294 (42.3)	126 (36.8)	199 (40.0)
30–34.9	298 (24.9)	221 (18.3)	210 (25.2)	126 (18.1)	88 (23.9)	95 (18.9)

	All participants		White participants		Black participants	
Characteristic	**Cases (N=1,217)**	**Controls (N=1,235)**	**Cases (N=856)**	**Controls (N=712)**	**Cases (N=361)**	**Controls (N=523)**
35+	230 (18.2)	147 (10.9)	156 (17.6)	74 (10.1)	74 (20.2)	73 (13.1)
Missing	13	8	8	2	5	6
History of hypertension						
Never	500 (40.8)	718 (59.0)	398 (45.1)	445 (61.7)	102 (28.8)	273 (51.3)
Ever	701 (59.2)	508 (41.0)	445 (55.0)	262 (38.3)	256 (71.2)	246 (48.7)
Missing	16	9	13	5	3	4
History of diabetes						
Never	1,017 (83.7)	1,065 (86.8)	733 (85.5)	633 (88.7)	284 (78.8)	432 (81.4)
Ever	200 (16.3)	169 (13.2)	123 (14.5)	78 (11.3)	77 (21.2)	91 (18.6)
Missing	0	1	0	1	0	0
Family history of cancer[c]						
None	517 (42.0)	566 (42.3)	334 (38.6)	278 (38.0)	183 (51.7)	288 (54.3)
Cancer other than kidney	636 (53.8)	633 (55.8)	484 (57.5)	413 (59.8)	152 (43.0)	220 (44.4)
Kidney cancer	52 (4.3)	24 (2.0)	33 (3.9)	15 (2.2)	19 (5.3)	9 (1.3)
Missing	12	12	5	6	7	6

[a]Reported as frequencies and sample-weighted percentages within each category.

[b]Based on current height and weight five years before interview.

[c]Among 1st degree relatives.

Table 2

Risk of renal cell carcinoma in relation to chronic renal failure, dialysis, and kidney transplantation

	Cases (%)[a]	Controls (%)[a]	Partially adjusted OR (95% CI)[b]	Fully adjusted OR (95% CI)[c]
Chronic renal failure	51 (4.1)	12 (0.8)	5.5 (2.6–11.6)	4.7 (2.2–10.1)
Dialysis	37 (3.0)	3 (0.2)	21.7 (4.5–104)	18.0 (3.6–91)
Kidney transplant	15 (1.1)	0 (0)	$p<0.001$[d]	---

[a] Frequencies and sample-weighted percentages, excluding subjects with missing information for history of chronic renal failure, dialysis, kidney transplantation, or other covariates in the fully adjusted model.

[b] Adjusted for matching variables (age, sex, race, and study center). We excluded subjects with missing information for any covariates, including those in the fully adjusted model.

[c] Adjusted for matching variables and level of education, smoking status, BMI, history of hypertension, and family history of cancer. Subjects with missing information for any covariates were excluded.

[d] P-value for chi-squared test of sample-weighted frequencies. Results were similar for unweighted Fisher's exact tests.

Table 3

Stratified analyses of risk of renal cell carcinoma in relation to chronic renal failure

	Cases (%)[a]	Controls (%)[a]	Partially adjusted OR (95% CI)[b]	Fully adjusted OR (95 % CI)[c]	P_{int}[d]
Race					
White	11 (1.4)	5 (0.7)	2.2 (0.8–6.4)	2.0 (0.7–5.6)	0.03
Black	40 (11.6)	7 (1.2)	10.6 (4.2–26.8)	8.7 (3.3–22.9)	
Sex					
Female	18 (3.5)	5 (0.7)	5.3 (1.6–17.1)	4.2 (1.3–13.7)	0.94
Male	33 (4.4)	7 (0.9)	5.5 (2.2–14.0)	4.9 (1.9–12.5)	
Age at RCC diagnosis					
20–64 years	41 (4.9)	6 (0.7)	7.3 (2.8–19.3)	6.1 (2.3–16.3)	0.35
≥65 years	10 (2.7)	6 (0.9)	3.1 (1.0–9.7)	3.5 (1.1–11.0)	
Time after diagnosis of chronic renal failure					
< 10 years	31 (2.4)	10 (0.7)	3.9 (1.7–9.0)	3.1 (1.3–7.3)	0.79
≥10 years	19 (1.5)	2 (0.1)	12.7 (1.4–114)	11.9 (1.4–102)	
History of diabetes					
No diabetes	34 (3.5)	5 (0.4)	9.3 (3.3–26.5)	8.3 (3.1–22.7)	0.03
Diabetes	17 (7.1)	7 (3.5)	2.0 (0.7–5.9)	1.9 (0.6–5.9)	

[a] Frequencies and sample-weighted percentages, excluding subjects with missing information for history of chronic renal failure or other covariates in the fully adjusted model.

[b] Adjusted for matching variables (age, sex, race, and study center). We excluded subjects with missing information for any covariates, including those in the fully adjusted model.

[c] Adjusted for matching variables and level of education, smoking status, BMI, history of hypertension, and family history of cancer. Subjects with missing information for any covariates were excluded.

[d] *P*-values for Wald tests of interaction between chronic renal failure and each stratifying variable in the fully adjusted models.