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HYPERTENSION AND RISK OF RENAL CELL CARCINOMA AMONG WHITE AND BLACK AMERICANS

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Abstract

BACKGROUND—Renal cell carcinoma and hypertension (a well-established renal cancer risk factor) are both more frequent among blacks than whites in the U.S. The association between hypertension and renal cell carcinoma has not been examined in black Americans. We investigated the hypertension–renal cancer association by race, and we assessed the role of hypertension in the racial disparity of renal cancer incidence.

METHODS—Participants were enrolled in a population-based case-control study in Detroit and Chicago during 2002–2007 (number of cases: 843 whites, 358 blacks; number of controls: 707 whites, 519 blacks). Participants reported their history of hypertension and antihypertensive drug use. We used unconditional logistic regression to calculate odds ratios (ORs) and 95% confidence intervals (CIs), adjusted for demographic characteristics, smoking, body mass index, and family history of cancer.

RESULTS—Hypertension doubled renal cancer risk (OR=2.0 [CI=1.7–2.5]) overall. For whites the OR was 1.9 (CI=1.5–2.4), while for blacks it was 2.8 (2.1–3.8) (p for interaction=0.11). ORs increased with time after hypertension diagnosis (p for trend <0.001), reaching 4.1 (CI=2.3–7.4) for blacks and 2.6 (CI=1.7–4.1) for whites after 25 years. ORs for poorly controlled hypertension were 4.5 (CI=2.3–8.8) for blacks and 2.1 (CI=1.2–3.8) for whites. If these estimates correctly represent causal effects and if, hypothetically, hypertension could be prevented entirely among persons aged 50–79 years, the black/white disparity in renal cancer could be reversed among women and reduced by two-thirds among men.

CONCLUSIONS—Hypertension is a risk factor for renal cancer among both blacks and whites, and might explain a substantial portion of the racial disparity in renal cancer incidence. Preventing and controlling hypertension might reduce renal cancer incidence, adding to the known benefits of blood pressure control for heart disease and stroke reduction, particularly among blacks.

Renal cell carcinoma (renal cancer) occurs more frequently among blacks than whites in the United States. According to population-based data from the U.S. Surveillance, Epidemiology, and End Results (SEER) program, renal cancer incidence rates in 2002–2005

were 19% higher for black men than white men (17.0 and 14.3 per 100,000 person-years, respectively, age-adjusted to the 2000 U.S. standard) and 4% higher for black women than white women (7.5 and 7.2 per 100,000, respectively).¹ Hypertension, which is a well-established risk factor for renal cancer, is more prevalent among blacks than whites.² Data from the National Health and Nutrition Examination Survey (NHANES) in 1999–2004 show age-adjusted prevalences of 39% and 28% for black and white men, respectively, and 41% and 27% for black and white women.³ We investigated the association between hypertension and renal cancer risk for blacks and whites, and assessed the role that hypertension might play in the racial disparity of renal cancer incidence.

METHODS

Study population

The U.S. Kidney Cancer Study was conducted in Detroit, Michigan (Wayne, Oakland, and Macomb Counties) and Chicago, Illinois (Cook County). All men and women newly diagnosed with histologically-confirmed adenocarcinoma of the renal parenchyma (renal cell carcinoma [ICD-O3-C64.9]) at ages 20 to 79 years were eligible for study. In Detroit, cases were identified through the Metropolitan Detroit Cancer Surveillance System (a SEER program member) between February 2002 and July 2006 (whites) or January 2007 (blacks). In Chicago, cases were diagnosed in 2003 through review of pathology reports at Cook County hospitals. Eligible controls were selected from the general population in the same counties as the cases, and frequency matched to cases on age (5-year intervals), sex, and race. Controls were identified from Department of Motor Vehicle (DMV) records (ages 20 to 64 years) and Medicare eligibility files (ages 65 to 79 years).

Although renal cancer incidence rates are higher among blacks than whites, more white than black renal cancer cases were diagnosed in the study catchment areas, which was expected given the greater number of white residents. Therefore, our power to conduct race-specific analyses was limited by the number of black participants. We designed a sampling strategy (eAppendices A and B, <http://links.lww.com>) to recruit sufficient numbers of black cases and controls efficiently, i.e., without exceeding recruitment goals for whites. To maximize the number of black cases, we sampled blacks completely while sampling at lower rates within some strata (age-race-sex combinations) of white cases. To further increase power for analyses restricted to blacks, we maintained a control:case matching ratio of 2:1 for blacks throughout the study. For whites, with larger numbers of cases, there was less need for additional power; we therefore matched at a ratio of 1:1.

Information on race was unavailable in the DMV records, but addresses were available. To increase sample yields of black controls, potential controls under age 65 (sampled from the DMV listings) were assigned to two sample strata based on whether they lived in a Census block group with a high or low percentage of black residents according to 2000 Census data. We oversampled people in areas with a high percentage of black residents to help achieve the targeted matching ratios for blacks under age 65. Allowance for effects on precision arising from this oversampling was made when setting sample sizes to help achieve the targeted frequency matching ratios for the study.

Of 1,918 eligible cases identified, 171 died before contact or interview, 92 could not be located, and 21 moved out of the area; in addition, physicians of 63 declined to give permission to contact patients. Among the remaining 1,571 cases, 221 declined participation and 133 were not interviewed due to serious illness, impairment, or nonresponse after multiple contact attempts. Thus, 1,217 cases participated (77% of the 1,571 we attempted to recruit). Of 2,718 presumed eligible controls, 41 died before contact or interview, 345 were not locatable, and 63 had moved away. Among the 2,269 controls we attempted to recruit,

677 declined participation and 357 were not interviewed due to serious illness, impairment, or lack of response to multiple contact attempts. Thus, 1,235 eligible controls participated (54% of those we attempted to recruit). The study was approved by Institutional Review Boards at all institutions, and written informed consent was obtained from all participants before interview.

Assessment of hypertension and other exposure variables

Trained interviewers conducted computer-assisted personal interviews in participants' homes to elicit information on demographic variables, height and weight, medical history, smoking history, family history of cancer, and other potential risk factors. In a section of the interview focusing on hypertension, participants were asked if they had been told by a health professional that they had high blood pressure. Those responding in the affirmative were asked a series of questions, including age at diagnosis and treatments prescribed. To assess how well blood pressure was controlled, we tailored additional questions to two groups of hypertensive persons based on the number of times they reported having had their blood pressure measured after being diagnosed with hypertension. If blood pressure was measured more than 10 times, we asked whether their blood pressure was higher than their doctor wanted it to be "all or almost all of the time," "most of the time," "some of the time," or "almost never or never" between the year of hypertension diagnosis and two years prior to interview. If blood pressure was measured fewer than 10 times, we asked how many times a doctor said it was too high, and divided the reported number by the total number of times blood pressure was measured; we then mapped the percentages into the above categories.

A separate part of the interview focused on medication use. Participants were asked if they ever took prescription medication for high blood pressure or heart problems at least once a week for a month or longer. "Heart problems" were included because some heart conditions (e.g., arrhythmias) are often treated with antihypertensive drugs (e.g., beta blockers). Respondents were shown a list of drugs used to treat hypertension or heart problems and asked to identify the ones they took. If they identified only medications that do not lower blood pressure (e.g., nitroglycerin to treat angina), they were not classified as antihypertensive medication users. Participants were also asked if they used prescription diuretics or water pills for weight control or swelling.

Because exposures near the time of a cancer diagnosis are unlikely to be causal, and because hypertension can result from renal cancer,⁴ people first diagnosed with hypertension within the two years preceding the reference year (year of renal cancer diagnosis for cases, selection year for controls) were considered normotensive for this analysis (12 cases, 7 controls).

Statistical analysis

We estimated the risk of developing renal cancer by deriving adjusted odds ratios (ORs) and 95% confidence intervals (CIs) from multiple logistic regression models that included study center, age at reference date (20–24, 25–29, 30–34, 35–39, 40–44, 45–49, 50–54, 55–59, 60–64, 65–70, 75–79 years), self-reported race (white, black), sex, education (<12 years, high school graduate, some college, 4+ years of college), smoking history as of two years before the reference date (never, occasional [smoked more than 100 cigarettes but never smoked one cigarette daily for six months], regular former, regular current), body mass index (BMI, based on height at interview and weight five years prior to interview: <25, 25–<30, 30–<35, 35+ kg/m², unknown [n=20]), and history of cancer among first-degree relatives (none, cancer other than kidney cancer, kidney cancer, unknown [n=24]). The reference group comprised people who were never told by a health professional that they were hypertensive. Tests for trend were performed by treating categorical variables as

continuous: for level of blood pressure control, the categories were scored from 0 to 4; for years since hypertension diagnosis, the value for each category was equal to the median value among controls. Interactions between two variables were tested by including multiplicative terms for the variables in the logistic regression, testing for the joint significance of the additional terms using the Wald chi-square test that is appropriate for weighted data.⁵ Analyses were conducted with STATA (StataCorp, College Station, TX) software version 10.1 using procedures appropriate for sample-weighted data.⁶ We excluded 25 study participants (16 cases, 9 controls) whose blood pressure was never measured or who could not remember whether they were ever diagnosed with hypertension, leaving 1,201 cases and 1,226 controls for analysis.

We developed sample weights to reduce the potential for bias arising from differential sampling rates for controls and cases, survey nonresponse, and deficiencies in coverage of the population-at-risk in the DMV and Medicare files. Sample weights for controls also included a post-stratification adjustment, so that the weighted distribution of controls across the matching variables matched exactly the weighted distribution of cases. In addition to being consistent with the objectives of the frequency matching, the post-stratification adjustment reduces the variability of the weights.⁷ We estimated the risk of developing renal cancer by deriving odds ratios and 95% confidence intervals from multiple logistic regression models using the post-stratification weights. Jackknife replicate weights were created to estimate standard errors for the calculation of 95% confidence intervals and computation of test statistics and p-values in the weighted risk analyses.⁸ For comparison, unweighted results are shown in eAppendixC (eTables C-1 through C-5; <http://links.lww.com>).

We calculated population attributable risk (PAR) to estimate the portion of the black excess in renal cancer incidence attributable to hypertension, separately for men and women. Chicago was excluded because of the small number of participants and the lack of SEER renal cancer incidence rates. Persons younger than age 50 were excluded because of the low occurrence of both hypertension and renal cancer. We computed race- and sex-specific PARs and standard errors for 806 cases and 798 controls using a sample-weighted version of the Bruzzi method,⁹ which is applicable to population-based case-control studies (as described in Graubard and Fears¹⁰) and recommended by Benichou¹¹ as an appropriate method for estimating adjusted PARs. We used the same adjustment factors and sampling weights as in the main analysis.

RESULTS

Black and white controls had more years of education than their respective cases (Table 1). Cases of each race had higher BMIs than controls and were more likely than controls to be current smokers, to report a history of hypertension, and to report kidney cancer among first-degree relatives.

For the study population overall, hypertension was associated with a two-fold risk of renal cancer (OR=2.0 [95% CI= 1.7 – 2.5]) (Table 2). Risk increased with the number of years since hypertension diagnosis (P for trend<0.001), reaching an OR of 2.9 (CI= 2.0 – 4.1) more than 25 years after hypertension was first diagnosed. Hypertensive persons with well-controlled blood pressure had a 60% increase in renal cancer risk (OR=1.6 [CI= 1.2 – 2.1]) compared with people who did not have hypertension; risk increased as the degree of blood pressure control decreased (P for trend<0.001), reaching an OR of 2.6 (1.9 – 3.7) if blood pressure was rarely controlled adequately.

Among black study participants, hypertension nearly tripled the risk of developing renal cancer (OR=2.8 [CI= 2.1 – 3.8]) (Table 2). We observed a four-fold risk (CI= 2.3 – 7.4) of renal cancer among blacks whose hypertension was diagnosed more than 25 years before the reference date, and an OR of 4.5 (2.3 – 8.8) if blood pressure was almost never controlled adequately. Hypertensive whites also had an elevated renal cancer risk, although the OR was lower than for blacks (1.9 [CI= 1.5 – 2.4] for whites; P for interaction = 0.11). As with blacks, marked trends were observed with years since hypertension diagnosis and level of blood pressure control. Stratification by both race and sex (eAppendixD, <http://links.lww.com>) showed that, for each measure of hypertension considered, the ORs were generally highest for black women (3.7 [2.0 – 7.1] for ever diagnosed with hypertension; 7.3 [3.0 – 18] if >25 years between first hypertension diagnosis and reference date; 6.6 [2.4 – 18] if hypertension was almost never controlled adequately).

Time since hypertension diagnosis and level of blood pressure control independently influenced renal cancer risk (Table 3). Regardless of the time since hypertension diagnosis, renal cancer risk was higher if blood pressure was poorly controlled than if it was well controlled. Among people with generally well-controlled hypertension, renal cancer risk increased with increasing years since hypertension diagnosis, reaching an OR of 2.6 (CI= 1.7 – 3.9) for periods longer than 25 years. The highest renal cancer risk was observed among those diagnosed with hypertension more than 25 years before the reference date, whose blood pressure was poorly controlled (3.4 [1.9 – 6.3]). For most combinations of time since hypertension diagnosis and level of blood pressure control, relative risk estimates for blacks exceeded those for whites, although small numbers in some cells led to unstable estimates.

To examine the relationships among hypertension, use of antihypertensive medications, and renal cancer risk, we identified a referent group of people who had never been diagnosed with hypertension and never been prescribed drugs with antihypertensive properties for treatment of other conditions (e.g., angina, arrhythmia, swelling, weight control). Compared with this group, normotensive persons who took prescription drugs with antihypertensive properties did not have an increased renal cancer risk (1.0 [0.7 – 1.4]) (Table 4). Hypertensive persons who never took antihypertensive medications had a reduced renal cancer risk (0.4 [0.2 – 0.9]). Hypertensive individuals who took antihypertensive drugs had an elevated renal cancer risk (2.2 [1.8 – 2.7]). Patterns were similar among blacks and whites.

Among male Detroit residents aged 50–79 years, the black-to-white ratio in renal cancer incidence rates during the study period was 1.26 (62.1/100,000 per year for blacks, 49.1/100,000 for whites) (Table 5). The estimated PARs for hypertension were 44% for black men and 35% for white men. If these associations are causal, it would follow that in the absence of hypertension, the renal cancer incidence rate would be 44% lower for black men (34.7/100,000) and 35% lower for white men (31.8/100,000), reducing the black:white ratio to 1.09. This suggests that 66% of the racial disparity in renal cancer incidence among men might be attributable to hypertension. Renal cancer incidence rates were lower for women and the black-to-white ratio was smaller (1.05). Again, if the associations are causal, we estimate that in the absence of hypertension, renal cancer incidence could be reduced by 51% for black women and 30% for white women, resulting in higher estimated renal cancer incidence rates among whites (19.9/100,000) than blacks (14.7/100,000).

DISCUSSION

In this study, hypertension was associated with an elevated risk of renal cancer in both blacks and whites. Renal cancer risk increased with increasing time since hypertension

diagnosis in both races, with stronger effects in blacks. A similar pattern was observed for decreasing levels of blood pressure control. When both race and sex were considered, black women had the strongest association of hypertension with renal cancer.

We know of no previous studies that have considered the association of hypertension and renal cancer among blacks. The two-fold risk observed among whites is similar to findings from many cohort^{12–15} and case-control^{16–23} studies. Our finding of increasing renal cancer risk with decreasing blood pressure control is consistent with prospective cohort studies reporting higher renal cancer risks with higher blood pressure measurements at baseline.^{15,24–26} Furthermore, in a cohort of Swedish men, a reduction in blood pressure over time was associated with a decrease in renal cancer risk, suggesting that effective hypertension control may lower risk.²⁵ The effect of hypertension duration on renal cancer risk has been examined mainly in case-control studies, with some reports of higher risks at longer durations,^{18,21} some of no association,^{19,22,23} and some of higher risks at durations of ≤ 5 years.^{17,27} Our finding that years since hypertension diagnosis and level of blood pressure control both independently affect renal cancer risk appears new; we know of no other study with information on both factors.

The biologic mechanisms underlying the hypertension-renal cancer association are unclear; hypotheses include lipid peroxidation and formation of reactive oxygen species,^{1,28} and up-regulation of hypoxia-inducible factors due to the chronic renal hypoxia that accompanies hypertension.^{1,15,29–31}

We compared hypertension histories among controls to the U.S. population using NHANES data (1999–2004).³ For consistency, we considered NHANES participants to be hypertensive only if they were already aware of their condition at the time of interview. The prevalence of hypertension among controls aged 50–79 years was comparable to that estimated based on NHANES data; differences within race and sex subgroups were generally small (black men: 55% in NHANES vs. 53% in our study; white men: 37% vs. 43%; black women: 63% vs. 58%; white women: 43% vs. 36%). For ages 20–49 years, when the occurrence of hypertension is low, the differences were pronounced for black men (11% in NHANES vs. 27% in our study) and black women (17% in NHANES vs. 6% in our study). Excluding those younger than age 50 from our analysis raised ORs for black men and lowered ORs for black women, but did not alter our conclusions. This provides evidence that our results are unbiased.

A source of controversy has been whether the hypertension-renal cancer association arises from the hypertension itself or from the use of antihypertensive medications. Although antihypertensive drugs have been associated with elevated renal cancer risk, recent studies have concluded that this is likely confounded by a history of hypertension.^{1,12,15,25,32,33} Renal cancer risk was not elevated among 156 normotensive individuals in our study who took prescription drugs with antihypertensive properties for conditions other than hypertension. This observation supports the position that renal cancer risk is increased by hypertension rather than by its treatment. Our observation that renal cancer risks are highest when blood pressure is poorly controlled also suggests that hypertension is the responsible factor. Further analysis of data collected in this study will examine whether specific types of antihypertensive medications influence renal cancer risk.

In our study, most of the unmedicated hypertensive subjects had been diagnosed with hypertension only recently (60% within five years of the reference date, compared with 27% of individuals who were medicated). Their blood pressure, when first rechecked by the diagnosing health care provider, was often found to be acceptable (25%) or borderline (50%), possibly indicating that they were not truly hypertensive or that their condition was

mild enough to be controlled with life-style changes. It is, however, difficult to explain the reduced renal cancer risk that we observed among unmedicated hypertensives. Compliance with physician-recommended life-style changes might have protected against renal cancer, but this is speculative. This finding is also based on a relatively small number of cases and controls, and chance variation is possible.

If the hypertension-renal cancer relationship observed in our study is causal, our calculations provide a rough upper bound on the potential benefits of hypertension control. If, hypothetically, it were possible to prevent hypertension entirely, we estimate that, among those aged 50–79, renal cancer incidence could be reduced by 44% and 35% among black and white men, and that the male racial disparity in renal cancer incidence in this age group could be reduced by 66%. Among women, our analysis suggests that renal cancer incidence in the absence of hypertension could be reduced by 51% and 30% for blacks and whites, respectively, and that the racial disparity could be reversed, with white women having higher incidence rates than black women. Clearly, preventing hypertension entirely is not an achievable goal. However, these estimates illustrate the substantial role that hypertension likely plays in the black-white disparity in renal cancer incidence rates.

Our study is, to our knowledge, the first renal cancer case-control study with enough blacks to evaluate the hypertension-renal cancer risk relationship by race. Another strength is the detailed information on hypertension, allowing evaluation of renal cancer risk according to both time since hypertension diagnosis and extent of hypertension control. Information on smoking, BMI, and family history of cancer allowed adjustment for potential confounders. Histologically-confirmed cancers and a large sample size are additional strengths.

An important limitation of the study was the need to rely on binary classification of hypertension because information on the severity of hypertension (blood pressure measurements, for example) was unavailable. NHANES data from 1999–2002 show that hypertensive blacks had slightly higher blood pressures than hypertensive whites (142/79 vs. 140/75, respectively), with a wider gap among the subset taking antihypertensive medication (141/77 for blacks, 137/72 for whites).³⁴ If renal cancer risk is higher for people with higher blood pressure, as evidence suggests,^{15,24–26} the higher blood pressures among hypertensive blacks (especially those with inadequate treatment) could explain the higher odds ratios observed among blacks compared with whites.

Another limitation is that hypertension and medication histories were based on self-report. Some hypertensive persons were likely unaware of their condition.³ We addressed this to some extent by excluding those whose blood pressure was never measured. If more cases than controls were aware of their hypertension, we might have overestimated the hypertension-renal cancer association and the PARs. However, the similarity of our risk estimates to those observed in cohort studies based on blood pressure measurements suggests that this source of bias was relatively minor.

Our study is also limited by the low response rate among controls, which is typical of recent population-based case-control studies. The use of sample weights helps to reduce the potential for bias arising from nonresponse, as the weights account for differential nonresponse across subgroups defined by factors (such as age, sex, and county of residence) for which data were available for both respondents and nonrespondents. That the hypertension history reported by our controls was comparable to that of NHANES suggests that selection bias was likely minimal.

Finally, comprehensive consideration of the interplay among race, hypertension, and renal cancer requires longitudinal information about blood pressure, anti-hypertensive medication use, weight and other potential confounders of the race-hypertension, hypertension-renal

cancer, and race-renal cancer associations.³⁵ Collection of data at this level of detail was not feasible in this population-based case-control study.

In conclusion, our study shows that hypertension is a risk factor for renal cancer among both blacks and whites. The stronger association observed among blacks using our crude definition of hypertension justifies more detailed assessment of hypertension in future studies. Reduction in risk of renal cancer may be a potential benefit of hypertension control, in addition to the known effects on heart disease and stroke, particularly in the black community.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1

Characteristics of cases and controls, by race, Kidney Cancer Study, Detroit and Chicago, 2002–2007^a

	Whites				Blacks			
	Cases (n=843)		Controls (n=707)		Cases (n=358)		Controls (n=519)	
	No.	(%) ^b	No.	(%) ^b	No.	(%) ^b	No.	(%) ^b
Study Site								
Chicago	115	(15)	99	(16)	79	(21)	96	(21)
Detroit	728	(85)	608	(84)	279	(79)	423	(79)
Age (years)								
20–44	103	(10)	93	(10)	40	(11)	84	(11)
45–54	180	(20)	145	(20)	102	(26)	124	(26)
55–64	254	(29)	205	(29)	117	(30)	145	(30)
65–74	218	(28)	193	(28)	81	(24)	132	(24)
75+	88	(13)	71	(12)	18	(8)	34	(8)
Sex								
Male	484	(62)	435	(62)	222	(61)	246	(60)
Female	359	(38)	272	(38)	136	(39)	273	(40)
Education								
<12 years	99	(12)	62	(9)	94	(27)	100	(19)
High school graduate	308	(36)	213	(31)	104	(29)	172	(33)
Some college	215	(25)	183	(26)	113	(31)	172	(32)
4+ years college	221	(26)	249	(34)	47	(13)	75	(15)
Body Mass Index (kg/m ²)								
<25	168	(19)	215	(29)	67	(19)	147	(27)
25–29.9	302	(37)	291	(42)	125	(36)	198	(40)
30–34.9	210	(25)	125	(18)	87	(24)	95	(19)
35+	156	(18)	74	(10)	74	(20)	73	(13)
Don't know	7	(1)	2	(<1)	5	(1)	6	(1)
Smoking Status								
Never	304	(36)	285	(40)	123	(34)	184	(35)
Occasional	34	(4)	25	(3)	21	(6)	30	(5)

	Whites				Blacks			
	Cases (n=843)		Controls (n=707)		Cases (n=358)		Controls (n=519)	
	No.	(%) ^b	No.	(%) ^b	No.	(%) ^b	No.	(%) ^b
Former	302	(37)	273	(39)	105	(29)	167	(34)
Current	203	(23)	124	(18)	109	(30)	138	(26)
Family History of Kidney Cancer								
None with cancer	329	(38)	276	(38)	180	(50)	284	(53)
Cancer other than kidney	476	(57)	410	(59)	152	(43)	220	(44)
Kidney cancer	33	(4)	15	(2)	19	(5)	9	(1)
Don't know	5	(1)	6	(1)	7	(2)	6	(1)
Ever Diagnosed with Hypertension								
No	398	(45)	445	(62)	102	(29)	273	(51)
Yes	445	(55)	262	(38)	256	(71)	246	(49)

^aExcludes 16 cases and 9 controls with unknown history of hypertension.

^bPercentages incorporate poststratification sample weights.

Table 2

Hypertension and renal cell carcinoma risk, by race

	All Participants ^a			Whites ^b			Blacks ^b		
	No. cases/controls	OR	(95% CI)	No. cases/controls	OR	(95% CI)	No. cases/controls	OR	(95% CI)
Ever diagnosed with hypertension									
No	500/718	1.0		398/445	1.0		102/273	1.0	
Yes	701/508	2.0	1.7–2.5	445/262	1.9	1.5–2.4	256/246	2.8	2.1–3.8
Years since hypertension diagnosis ^c									
Never had hypertension	500/718	1.7	1.4–2.6	398/445	1.0	1.2–2.4	56/77	1.0	
>0–5	180/160	1.9	1.7–3.3	124/83	1.7	1.3–2.6	68/69	1.9	1.2–2.9
6–15	215/154	2.3	2.0–4.1	147/85	1.8	1.3–3.0	65/45	2.6	1.7–4.0
16–25	158/100	2.9		93/55	2.0	1.7–4.1	66/55	4.0	2.3–6.7
26+	146/92	P<0.001		80/37	2.6			4.1	2.3–7.4
Test for trend									P<0.001
Blood pressure control ^d									
Never had hypertension	500/718	1.0		398/445					
Always well controlled	176/163	1.6		134/98	1.0		102/273	1.0	
Usually well controlled	293/204	2.0	1.2–2.1	175/101	1.6	1.2–2.3	42/65	1.6	0.98–2.6
Rarely well controlled	97/65	2.6	1.6–2.6	62/23	1.7	1.3–2.4	118/103	3.4	2.4–4.6
Almost never controlled	78/45	2.6	1.9–3.7	41/24	3.0	1.8–5.0	35/42	2.5	1.4–4.3
Test for trend									
		P<0.001	1.7–4.0		2.1	1.2–3.8	37/21	4.5	2.3–8.8
									P<0.001

^a Adjusted for study center, race, sex, age, education, smoking status, body mass index, and family history of kidney cancer^b Adjusted for the same variables as for all participants – except for race.^c Excludes 2 hypertensive cases and 2 hypertensive controls with unknown years since hypertension diagnosis^d Excludes 57 hypertensive cases and 31 hypertensive controls with unknown blood pressure control

Table 3

Odds ratios for renal cell carcinoma by years since hypertension diagnosis and level of blood pressure control

Blood Pressure Control	Years Since Hypertension Diagnosis					
	<=5		6-15		16-25	
	No. cases/controls	OR (95% CI)	No. cases/controls	OR (95% CI)	No. cases/controls	OR (95% CI)
All Participants ^b						
Well controlled ^c	123/113	1.6 (1.1-2.2)	150/120	1.6 (1.2-2.2)	113/72	2.2 (1.5-3.2)
Poorly controlled ^d	34/31	1.9 (1.1-3.3)	52/32	2.8 (1.6-4.6)	41/25	2.7 (1.5-4.9)
Whites ^e						
Well controlled ^c	87/61	1.6 (1.04-2.4)	108/70	1.6 (1.1-2.3)	65/42	1.7 (1.1-2.7)
Poorly controlled ^d	22/14	1.9 (0.9-4.2)	30/14	2.4 (1.1-5.0)	26/12	2.8 (1.2-6.4)
Blacks ^e						
Well controlled ^c	36/52	1.9 (1.2-3.1)	42/50	2.0 (1.2-3.3)	48/30	4.4 (2.5-7.9)
Poorly controlled ^d	12/17	2.0 (0.9-4.3)	22/18	4.2 (2.1-8.2)	15/13	3.0 (1.2-7.3)
					23/15	3.7 (1.5-9.2)

^a Referent group is respondents with no history of hypertension (500 cases, 718 controls). Table excludes 57 cases and 31 controls with unknown years since hypertension diagnosis or unknown level of blood pressure control.

^b Adjusted for study center, race, sex, age, education, smoking status, body mass index, and family history of kidney cancer

^c Participant reported that blood pressure was higher than the doctor wanted it to be "some of the time" or "almost never or never." If participant answered in terms of the number of times blood pressure was too high, we estimate that blood pressure was too high ≤50% of the time.

^d Participant reported that blood pressure was higher than the doctor wanted it to be "most of the time" or "all or almost all of the time." If participant answered in terms of the number of times blood pressure was too high, we estimate that blood pressure was too high >50% of the time.

^e Adjusted for study center, sex, age, education, smoking status, body mass index, and family history of kidney cancer

Table 4
Hypertension, use of prescription antihypertensive medications, and renal cell carcinoma risk, by race

Ever Diagnosed with Hypertension	Ever Took Prescription Antihypertensive Medication ^b	All Participants ^c			Whites ^d			Blacks ^d		
		No. Cases/Controls	OR	(95% CI)	No. Cases/Controls	OR	(95% CI)	No. Cases/Controls	OR	(95% CI)
No	No ^e	427/621	1.0	--	341/386	1.0	--	86/235	1.0	--
	Yes	69/87	1.0	(0.7–1.4)	55/54	1.0	(0.7–1.5)	14/33	1.1	(0.5–2.2)
Yes	No	14/38	0.4	(0.2–0.9)	9/25	0.4	(0.2–0.96)	5/13	0.7	(0.2–2.7)
	Yes	682/467	2.2	(1.8–2.7)	433/236	2.0	(1.6–2.7)	249/231	3.0	(2.2–4.2)

^a Excludes 9 cases and 13 controls with unknown use of antihypertensive medications

^b For high blood pressure, heart problems, weight control, or swelling

^c Adjusted for study center, race, sex, age, education, smoking status, body mass index, and family history of kidney cancer

^d Adjusted for same variables as for all participants, except for race.

^e Reference category.

Table 5

Population attributable risk (PAR) for hypertension and contribution of hypertension to black excess in renal cell carcinoma incidence, Detroit residents aged 50–79 years

Race and Sex	Population Attributable Risk for Hypertension ^a %	Renal Cell Carcinoma Incidence Rate (per 100,000 per year)	
		SEER Rate ^b	Calculated Rate in the Absence of Hypertension ^c
Black Men	44	62.1	34.7
White Men	35	49.1	31.8
		Black:white ratio = 1.26	Black:white ratio = 1.09
Black Women	51	29.8	14.7
White Women	30	28.3	19.9
		Black:white ratio = 1.05	Black:white ratio = 0.74

^a Adjusted for age, education, smoking status, body mass index, and family history of kidney cancer, weighted

^b Microscopically-confirmed cases of adenocarcinoma of the kidney (renal parenchyma) or renal pelvis at ages 50–79, Detroit SEER, 2002–2006 (22)

^c Renal cancer incidence rate in the absence of hypertension (i.e., if nobody had a history of hypertension) = SEER rate x (1-PAR)