Research Article

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Cigarette Smoking and Renal Cell Carcinoma Risk among Black and White Americans: Effect Modification by Hypertension and Obesity

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Abstract

Background: Incidence of kidney cancer has been increasing over the past three decades, with more rapid increases and higher incidence rates among blacks than whites in the United States. An association between cigarette smoking and renal cell carcinoma (RCC), the most common form of kidney cancer, has been reported for whites, but the association in blacks is less clear.

Methods: The association between smoking and RCC was examined in 1,217 incident cases and 1,235 population controls frequency-matched on age, race, gender, and study site in the Kidney Cancer Study in Detroit, MI, and Chicago, IL.

Results: In white individuals, increasing duration and number of pack-years of both were associated with increased risk of RCCs after adjusting for age, gender, education, study site, body mass index (BMI) and history of hypertension ($P_{trend} = 0.0002$ and $P_{trend} = 0.002$, respectively). Among black individuals, RCC risk increased with duration of smoking ($P_{trend} = 0.02$) but not other measures. Compared with current smokers, RCC risk decreased with increasing years of smoking cessation among both whites and blacks ($P_{trend} = 0.01$ and 0.02, respectively). When examining risk according to hypertension history, associations between smoking and RCC risk were observed only among individuals who reported never having been diagnosed with hypertension. Similarly, cigarette smoking was associated with increased risk of RCCs among nonobese individuals but not among those with BMI ≥ 30 kg/m^2.

Conclusion: Our observation that smoking is associated with RCC only in nonobese individuals and those with no history of hypertension are novel findings.

Impact: The complex relationships between RCCs, smoking, hypertension, and obesity require additional confirmation. *Cancer Epidemiol Biomarkers Prev; 21(5); 770–9. ©2012 AACR.*

Introduction

Kidney cancer is one of the top 10 most commonly diagnosed cancers in men and women in the United States (1). Data from 2004 to 2008 gathered by the National Cancer Institute's Surveillance, Epidemiology and End Results (SEER) database show a higher age-adjusted incidence of kidney cancer among black men (23.3 per 100,000) and women (11.6 per 100,000) than among white men and women (20.7 per 100,000 and 10.5 per 100,000, respectively; ref. 1). Incidence rates for both sexes have been increasing over the past 3 decades, with a more rapid increase among blacks than among whites in the United States (1).

The strongest known risk factors for kidney cancer are hypertension and obesity (2). The prevalence of both conditions has been increasing more quickly in blacks than in other racial and ethnic groups (3, 4). Cigarette smoking has been linked to increased risk of several cancers, including renal cell carcinoma (RCC), the most common form of kidney cancer (5). Still, more than 20% of the adult U.S. population report being current smokers (6). In addition, former smokers remain at increased risk for many cancers years after smoking cessation (7). The association between cigarette smoking and kidney cancer has been examined by gender (8–15), but no studies have published this association by race.

Currently, the prevalence of smoking is similar for black and white men, with about a quarter of adult men reporting current smoking, although in the past, smoking prevalence was higher among black men (16). Current smoking is less common among women of both races (~20%) and more frequent among white women (16). Black

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smokers generally smoke fewer cigarettes than white smokers and are also more likely to smoke mentholated cigarettes (17, 18), have higher serum cotinine levels (19), and higher intake of nicotine per cigarette (20).

In the present study of 1,217 incident cases of RCCs and 1,235 population-based controls, we examine the relationship between cigarette smoking and RCC risk. Because of the racial differences identified in incidence rates and trends, we are particularly interested in examining this association by race, considering both hypertensive status and body mass index (BMI).

Materials and Methods

Study population

The Kidney Cancer Study is a population-based case–control study conducted in the metropolitan areas of Detroit, MI (Wayne, Oakland, and Macomb counties) and Chicago, IL (Cook County). Details about the study design can be found in the study by Colt and colleagues (21). Briefly, eligible cases were resident white and black men and women ages 20 to 79 years, newly diagnosed with RCC (ICD-O topography code = C64.9, morphology codes = 8140, 8255–8323, 8959). In Detroit, cases were diagnosed on or after February 1, 2002, through July 31, 2006, for whites and through January 31, 2007, for blacks. Cases in Detroit were identified through the Metropolitan Detroit Cancer Surveillance System, a SEER program member. In Chicago, cases were diagnosed on or after January 1, 2003, through December 31, 2003, and were identified by reviewing pathology reports at hospitals in Cook county. The investigators designed a complex sampling strategy that allowed recruitment of sufficient numbers of black cases and controls without exceeding recruitment goals for whites, yet allowed unbiased estimators and accurate confidence intervals (21). All black cases were recruited, whereas some strata (age/gender combinations) of white cases were sampled at lower rates. In addition, to increase the power for analyses restricted to blacks, a 2:1 control:case ratio was maintained for blacks. A 1:1 ratio was deemed sufficient for white cases and controls.

Eligible controls were selected from the general population by the coordinating center, Westat, Inc., and were frequency-matched to cases on age (5-year intervals), gender, and study center. Controls ages 65 to 79 years were identified from Medicare eligibility files. Controls ages less than 65 years were identified from motor vehicle (DMV) records. Information on race was unavailable in the DMV records but home address was available. To increase the sample yields of black controls, people living in areas with a high density of black residents (based on 2000 Census data) were oversampled to help achieve the targeted matching ratios for blacks. All local Institutional Review Boards approved this study.

Data collection and variable definitions

Trained interviewers conducted in-person meetings to complete the informed consent process before administering a computer-assisted personal interview (CAPI). The interview consisted of demographic information, medical history, self-reported adult height and weight at several different ages, adult diet, occupational history, tobacco use, and other potential risk factors. Hypertension history was self-reported, based on whether they had been diagnosed with hypertension by a health professional more than 2 years before the reference date. This time point was used to reduce any potential recall or reporting bias by the cases due to their RCC diagnosis.

Nonsmokers were individuals who reported smoking less than 100 cigarettes in their lifetime. Individuals were classified as "occasional" smokers if they smoked more than 100 cigarettes in their lifetime but had never smoked at least one cigarette a day for 6 months or longer. Individuals who smoked more than 100 cigarettes, and who smoked at least one cigarette a day for at least 6 months, were classified as either current or former smokers based on their smoking status 2 years before the reference date (date of case diagnosis or control selection). Pack-years were calculated by multiplying the number of cigarettes smoked per day by the number of years of smoking (minus the number of years reported as having not smoked during the period) divided by 20. Former and current smokers were further categorized into light and heavy smokers using the median number of pack-years in the control population (20 pack-years) as the cutoff point. Current smoking status and number of pack-years of smoking were combined to create a smoking history variable. Analyses examining age at smoking initiation and cessation do not include nonsmokers.

Of 1,918 eligible cases identified during the study period, 171 died before contact or interview, 92 could not be located with the available contact information, 21 moved out of the area, and the physicians of 63 cases refused permission to contact their patients. Among the remaining 1,571 cases we sought to enroll, 221 declined participation and 133 were not interviewed because of serious illness, impairment, or not responding to multiple attempts to contact, and race was unknown for 11 cases. Thus, 1,217 cases we attempted to recruit participated in the study (77.5% of white cases and 79.3% of black cases, 63.5% of all identified cases). Of 2,718 presumed eligible controls, 41 died before contact or interview, 345 could not be located with the available contact information, and 63 had moved out of the region. Among the 2,269 controls we attempted to recruit, 677 declined to participate and 357 were not interviewed because of serious illness, impairment, or not responding to multiple attempts to contact. Thus, 1,235 eligible controls we attempted to recruit participated in the study (53.3% of presumed white controls and 55.9% of presumed black controls, 45.4% of all identified potential controls).

Statistical analysis

Details about sample weights are given in the article by Colt and colleagues (21) and were implemented to reduce the potential for bias from differential sampling rates for

controls and cases but also nonparticipation and deficiencies in coverage of the population at-risk arising from use of the DMV and Medicare files as sampling frames (22). The sample weights for the controls included a post-stratification adjustment, which resulted in identical distributions between the cases and controls for the matching variables (age, gender, and study center) and reduces the variability of the weights (22). The effect of cigarette smoking on RCC risk was evaluated in unconditional logistic regression models, adjusting for study site (Chicago or Detroit), reference age (20–44, 45–54, 55–64, 65–74, 75+ years), race (white/black), BMI 5 years before interview (<25, 25–<30, 30–<35, 35+ kg/m^2), years of education (less than high school diploma, high school diploma or equivalent, some college, 4-year college degree or more), and history of hypertension (ever/never). ORs and 95% confidence intervals (CI) were calculated from multiple logistic regression models using the post-stratification weights. Jackknife replicate weights were created to estimate SEs and P values in the weighted risk analyses (23–25). Analyses were repeated after stratification by race, BMI (<30 kg/m^2, 30+ kg/m^2), and history of hypertension (ever/never). For nonordered categorical variables (smoking status and smoking history), an overall test for significance was conducted using the Wald test. For ordered variables (number of years smoked, average number of cigarettes per day, pack-years, age at smoking initiation, and years since quitting), tests for trend were assessed only among the exposed. These tests for trend were conducted by including the categorical variable of interest in the model, with the categories scored using the middle value of each category. Modification of smoking effect by hypertension or BMI was assessed by adding an interaction term to the unconditional logistic regression model, separately for blacks and whites. Sensitivity analyses were conducted to assess whether results differed when only Detroit subjects (83.9% of the study population) or those with clear cell histology (73.8% of case subjects) were included. Results were considered to be statistically significant at $\alpha = 0.05$, and all reported P values are 2-sided. SAS Version 9.2 (SAS Institute Inc.), using procedures appropriate for sample-weighted data, was used for all analyses (25).

Results

The raw numbers and weighted percentages of demographic characteristics, hypertension status, and BMI category are presented by race and case–control status in Table 1. The analyses included 361 black cases and 523 black controls and 856 white cases and 712 white controls. Both white and black cases were more likely to have higher BMIs than controls ($P < 0.0001$ and $P = 0.0004$, respectively) and to report a history of hypertension (both $P < 0.0001$). Controls were more likely than cases to have some college or a 4-year college degree ($P = 0.0003$ and $P = 0.05$, respectively). The majority of the participants had clear cell cancers (77.7% of white and 64.1% of black cases). Further clinical details for this population are described by Miller and colleagues (26).

Compared with whites who never smoked, white current smokers had a significantly increased risk of RCC after adjusting for age, study center, gender, education, BMI, and hypertension (OR, 1.46; 95% CI, 1.05–2.04; Table 2). Among whites who reported smoking, RCC risk increased significantly as pack-years of smoking increased ($P_{trend} = 0.002$), and decreased significantly with increasing years of smoking cessation ($P = 0.01$). White individuals who were classified as current heavy smokers were significantly more likely to have RCCs than those who never smoked (OR, 1.62; 95% CI, 1.12–2.34).

Blacks who were current smokers had a slightly elevated, but nonsignificant, risk of RCC compared with blacks who never smoked (OR, 1.16; 95% CI, 0.81–1.65) after adjustment. Among blacks who ever smoked, number of years of smoking was associated with RCC risk ($P_{trend} = 0.02$), but the relative risks for each stratum were modest for even the longest durations (for 41+ years: OR, 1.22; 95% CI, 0.72–2.07). As with whites, RCC risk decreased with increasing years of smoking cessation ($P = 0.02$). Neither race showed an association between average number of cigarettes smoked per day or age at smoking initiation and RCC risk; thus, these variables were not considered in other stratified analyses.

The association between smoking and RCC risk stratified by hypertension and race is shown in Table 3. Among whites who reported no history of hypertension (i.e., normotensives), significant associations with RCCs were observed for smoking duration ($P_{trend} = 0.005$) and pack-years ($P_{trend} = 0.004$). Current heavy smokers who were normotensive had a nearly 2-fold risk of RCC (OR, 1.89; 95% CI, 1.21–2.96). Among normotensive blacks, RCC risk also increased significantly with duration of smoking ($P_{trend} = 0.03$). Regardless of race, smoking was not associated with RCCs in those reporting a history of hypertension. Significant interactions were not detected between effects of smoking and hypertension (data not shown).

The association between RCCs and cigarette smoking is examined by BMI and race in Table 4. Among nonobese white individuals, both the number of years smoked ($P_{trend} < 0.0001$) and pack-years of smoking ($P_{trend} = 0.0002$) were significantly associated with RCCs. For nonobese black smokers, number of years smoked was associated with RCCs ($P_{trend} = 0.005$). Length of smoking cessation was associated with a reduction of risk compared with current smokers ($P_{trend} = 0.008$), with a 70% reduction in risk among those with 25+ years of smoking cessation (OR, 0.29; 95% CI, 0.13–0.65). There were no associations between any of the smoking variables and RCC risk in obese whites or blacks. The interaction between pack-years of smoking and BMI was significant among whites ($P_{interaction} = 0.02$ for whites and 0.15 for blacks). Using an intensity variable for smoking, number of cigarettes smoked per day, the interaction with BMI

Table 1. Demographic and risk factor characteristics among RCC study subjects, by race

	White		Black	
	Cases (N = 856) Weighted%	Controls (N = 712) Weighted%	Cases (N = 361) Weighted%	Controls (N = 523) Weighted%
Study site				
Chicago	118 (15.1)	101 (16.1)	81 (21.4)	96 (21.0)
Detroit	738 (84.9)	611 (83.9)	280 (78.6)	427 (79.0)
Age, y				
20–44	106 (10.1)	93 (10.1)	41 (11.6)	86 (11.6)
45–54	185 (20.0)	145 (20.0)	102 (26.1)	125 (26.1)
55–64	255 (29.1)	205 (29.1)	117 (30.2)	145 (30.2)
65–74	211 (28.1)	196 (28.1)	82 (24.3)	133 (24.3)
75+	89 (12.7)	73 (12.7)	19 (7.9)	34 (7.9)
Gender				
Men	495 (62.0)	439 (61.6)	225 (61.2)	250 (60.8)
Women	361 (38.0)	273 (38.4)	136 (38.8)	273 (39.2)
Education				
Less than diploma	103 (12.7)	65 (9.4)	97 (28.1)	100 (19.1)
High school diploma	315 (36.5)	214 (30.8)	104 (28.7)	176 (33.5)
Some college	215 (24.9)	184 (25.6)	113 (30.3)	172 (32.1)
4-year degree	223 (25.9)	249 (34.2)	47 (12.8)	75 (15.3)
BMI, kg/m^2				
<25	172 (19.4)	216 (29.4)	68 (18.8)	150 (27.9)
25–<30	310 (37.3)	294 (18.1)	126 (36.3)	199 (39.7)
30–<35	210 (25.0)	126 (11.8)	88 (23.6)	95 (18.7)
35+	156 (17.4)	74 (9.9)	74 (19.9)	73 (13.0)
Missing	8 (0.9)	2 (0.2)	5 (1.5)	6 (0.7)
Hypertension				
Never	398 (44.3)	445 (61.3)	102 (28.6)	273 (50.8)
Ever	445 (54.1)	262 (38.0)	256 (70.6)	246 (48.3)
Missing	13 (1.6)	5 (0.8)	3 (0.8)	4 (0.9)
Family history of RCCs				
No	823 (96.1)	697 (97.9)	342 (94.7)	514 (98.3)
Yes	33 (3.9)	15 (2.1)	19 (5.3)	9 (1.7)
Histology				
Clear cell	629 (73.4)	—	209 (57.6)	—
Papillary	82 (9.8)	—	72 (19.6)	—
Other[a]	99 (11.0)	—	45 (12.6)	—
Unknown	46 (5.9)	—	35 (10.2)	—
SEER summary stage				
Local	590 (67.5)	—	250 (70.4)	—
Regional	127 (14.9)	—	27 (7.0)	—
Distant	37 (4.5)	—	20 (5.9)	—
Unknown	102 (13.1)	—	64 (16.7)	—

NOTE: Percentages may not total to 100 due to rounding. All values are *n* (%).
[a]Other histology includes chromophobe, cystic, and other rare RCC subtypes.

was significant among both groups ($P_{interaction} = 0.03$ for whites and <0.001 for blacks). The effect of smoking on RCC risk is stronger among those with lower BMIs.

Sensitivity analyses were conducted to assess whether these results would differ if only Detroit subjects (83.9% of the study population) or those with clear cell histology (73.8% of case subjects) were included. No appreciable differences in the overall findings were noted in these subpopulations (data not shown).

Discussion

Our case–control study of more than 2,400 individuals, including 1,217 incident cases of RCCs, is the first to report

Table 2. ORs and 95% CIs for risk of RCC associated with smoking variables, by race

	White				Black			
	Cases[a]	Controls[a]	OR (95% CI)[b]	P_{trend}[c,d]	Cases[a]	Controls[a]	OR (95% CI)[b]	P_{trend}[c,d]
Smoking status				**0.04**				0.19
Never	309	287	1.00 (ref)		123	184	1.00 (ref)	
Occasional	34	25	1.51 (0.92–2.49)		21	30	1.02 (0.54–1.91)	
Former	304	276	0.99 (0.78–1.25)		106	169	0.81 (0.56–1.18)	
Current	209	124	**1.46 (1.05–2.04)**		111	140	1.16 (0.81–1.65)	
Number of years smoked[c]				**0.0002**				**0.02**
Never smoked	309	287	1.00 (ref)		123	184	1.00 (ref)	
≤9	57	67	0.90 (0.60–1.35)		13	28	0.49 (0.23–1.06)	
10–20	107	103	0.94 (0.66–1.34)		39	67	0.81 (0.47–1.41)	
21–30	103	90	0.92 (0.67–1.25)		54	76	1.07 (0.67–1.69)	
31–40	130	73	1.42 (0.98–2.06)		70	86	1.08 (0.70–1.68)	
41+	115	67	**1.58 (1.08–2.06)**		39	49	1.22 (0.72–2.07)	
Average no. of cigarettes/d[b,c]				0.59				0.89
Never smoked	309	287	1.00 (ref)		123	184	1.00 (ref)	
1–19	140	130	1.08 (0.79–1.47)		107	158	1.01 (0.69–1.46)	
20–39	277	201	1.21 (0.96–1.52)		89	131	0.87 (0.58–1.31)	
40+	96	67	1.12 (0.77–1.61)		20	19	1.25 (0.55–2.82)	
Pack-years[b,c]				**0.002**				0.72
Never smoked	309	287	1.00 (ref)		123	184	1.00 (ref)	
0.1–≤10.99	95	109	1.02 (0.76–1.36)		63	93	0.92 (0.63–1.36)	
11–20.00	79	80	0.93 (0.61–1.42)		46	81	0.89 (0.57–1.39)	
20.01–40.00	164	108	**1.29 (1.01–1.64)**		63	79	0.99 (0.65–1.50)	
40.01+	174	101	**1.38 (1.02–1.95)**		42	53	1.00 (0.59–1.69)	
Age at smoking initiation[e]				0.42				0.40
21+	76	66	1.00 (ref)		49	87	1.00 (ref)	
18–20	134	124	0.78 (0.54–1.14)		58	82	0.97 (0.57–1.66)	
16–17	132	94	1.01 (0.69–1.46)		51	69	0.96 (0.57–1.60)	
≤15	170	116	1.01 (0.69–1.50)		58	70	1.16 (0.65–2.07)	
Years since quitting[b,c,e]				**0.01**				**0.02**
Current smoker	209	124	1.00 (ref)		111	140	1.00 (ref)	
≤5	88	102	1.34 (0.83–2.17)		18	43	0.97 (0.51–1.85)	
6–15	77	83	0.82 (0.53–1.25)		25	41	0.73 (0.42–1.26)	
16–25	87	60	**0.61 (0.39–0.94)**		34	48	0.72 (0.38–1.37)	
25+	52	31	0.62 (0.39–1.01)		28	35	**0.47 (0.25–0.88)**	
Smoking history				**0.02**				0.32
Never smoked	309	287	1.00 (ref)		123	184	1.00 (ref)	
Occasional	34	25	1.51 (0.91–2.46)		21	30	1.00 (0.54–1.86)	
Former/light	140	157	0.91 (0.66–1.25)		54	102	0.73 (0.48–1.10)	
Current/light	34	32	1.01 (0.62–1.64)		55	72	1.30 (0.79–2.14)	
Former/heavy	164	117	1.17 (0.88–1.55)		51	65	0.97 (0.59–1.60)	
Current/heavy	174	92	**1.62 (1.12–2.34)**		54	67	1.07 (0.68–1.69)	

[a]Missing data: Number of years smoked: 1 white case, 2 black cases, 3 black controls. Number of cigarettes per day: 2 white controls, 1 black case, 1 black control. Pack-years could not be calculated for these 9 individuals (one person missing both variables). Years since quitting: 1 black case and 2 black controls.

[b]Adjusted for age, study site, gender, BMI, education, family history of kidney cancer in a first-degree relative, and hypertension (years since quitting also adjusted for pack-years).

[c]Occasional smokers are not included: 34 white cases, 21 black cases, 25 white controls, and 30 black controls.

[d]For smoking status and smoking history, this number represents the overall test of significance.

[e]Age at smoking initiation and years since quitting do not include nonsmokers.

Table 3. Adjusted ORs and 95% CIs for risk of RCCs associated with smoking variables, by hypertensive status and race

	White				Black			
	Cases	Controls	OR (95% CI)[a]	P_{trend}[a,b]	Cases	Controls	OR (95% CI)[a]	P_{trend}[a,b]
Normotensive								
Number of years smoked				**0.005**				**0.03**
Never smoked	137	181	1.00 (ref)		36	111	1.00 (ref)	
≤9	35	52	0.93 (0.55–1.56)		4	12	0.89 (0.23–3.40)	
10–20	54	63	1.06 (0.66–1.71)		11	45	0.72 (0.33–1.60)	
21–30	53	55	1.09 (0.71–1.68)		21	37	1.63 (0.78–3.43)	
31–40	59	40	**1.71 (1.05–2.81)**		18	40	1.37 (0.66–2.89)	
41+	44	30	**2.20 (1.26–3.86)**		9	12	2.97 (0.90–9.85)	
Pack-years				**0.004**				0.30
Never smoked	137	181	1.00 (ref)		36	111	1.00 (ref)	
0.1–≤10.99	55	80	0.95 (0.62–1.45)		17	45	1.18 (0.62–2.24)	
11–20.99	40	50	1.04 (0.60–1.82)		14	44	1.03 (0.49–2.15)	
21–40.99	82	62	**1.64 (1.12–2.41)**		18	41	1.25 (0.66–2.39)	
41+	68	46	**1.85 (1.09–3.13)**		13	16	2.29 (0.88–5.94)	
Years since quitting				0.07				0.10
Current	106	83	1.00 (ref)		37	73	1.00 (ref)	
<5	27	24	1.16 (0.59–2.27)		9	15	1.57 (0.45–5.43)	
6–15	46	32	1.06 (0.59–1.88)		8	23	0.52 (0.20–1.38)	
16–25	35	46	0.64 (0.37–1.12)		7	14	1.43 (0.51–4.00)	
25+	31	55	0.53 (0.25–1.14)		2	21	0.15 (0.01–1.75)	
Smoking history				**0.03**				0.66
Never smoked	137	181	1.00 (ref)		36	111	1.00 (ref)	
Occasional	16	24	0.94 (0.52–1.68)		3	14	0.60 (0.16–2.22)	
Former/light	76	103	1.02 (0.67–1.54)		14	48	0.93 (0.48–1.82)	
Current/light	19	27	0.85 (0.45–1.63)		17	41	1.22 (0.53–2.79)	
Former/heavy	63	52	1.51 (0.93–2.47)		12	25	1.33 (0.56–3.11)	
Current/heavy	87	56	**1.89 (1.21–2.96)**		19	32	1.58 (0.79–3.16)	
Hypertensive								
Number of years smoked				0.07				0.15
Never smoked	167	104	1.00 (ref)		87	73	1.00 (ref)	
≤9	22	15	0.91 (0.43–1.91)		9	15	0.40 (0.18–1.01)	
10–20	53	39	0.80 (0.47–1.36)		27	22	0.81 (0.36–1.81)	
21–30	46	34	0.71 (0.46–1.09)		32	39	0.72 (0.40–1.29)	
31–40	70	32	1.15 (0.69–1.90)		52	45	0.95 (0.55–1.64)	
41+	68	37	1.10 (0.70–1.74)		29	35	0.97 (0.53–1.77)	
Pack-years				0.28				0.92
Never smoked	167	104	1.00 (ref)		87	73	1.00 (ref)	
0.1–≤10.99	40	29	0.77 (0.43–1.38)		45	47	0.74 (0.45–1.23)	
11–20.00	38	28	0.77 (0.44–1.35)		32	35	0.85 (0.49–1.46)	
20.01–40.00	80	45	0.85 (0.59–1.23)		44	38	0.81 (0.48–1.35)	
40.01+	101	55	0.92 (0.61–1.37)		28	36	0.68 (0.37–1.25)	
Years since quitting				0.22				0.29
Current	97	41	1.00 (ref)		72	65	1.00 (ref)	
<5	25	7	1.97 (0.77–5.04)		19	19	0.83 (0.39–1.80)	
6–15	40	28	0.63 (0.34–1.18)		25	24	0.89 (0.45–1.75)	
16–25	41	36	0.63 (0.33–1.18)		18	27	0.64 (0.28–1.45)	
25+	57	45	0.86 (0.44–1.67)		16	22	0.72 (0.32–1.62)	
Smoking history				0.63				0.24
Never smoked	167	104	1.00 (ref)		87	73	1.00 (ref)	

(Continued on the following page)

Table 3. Adjusted ORs and 95% CIs for risk of RCCs associated with smoking variables, by hypertensive status and race (Cont'd)

	White				Black			
	Cases	Controls	OR (95% CI)[a]	P_{trend}[a,b]	Cases	Controls	OR (95% CI)[a]	P_{trend}[a,b]
Occasional	18	1	NA		18	16	1.19 (0.54–2.61)	
Former/light	64	52	0.78 (0.50–1.23)		40	53	0.62 (0.38–1.01)	
Current/light	14	5	1.81 (0.65–5.03)		37	29	1.35 (0.70–2.62)	
Former/heavy	99	64	0.86 (0.60–1.24)		38	39	0.86 (0.47–1.57)	
Current/heavy	82	36	1.17 (0.74–1.84)		34	35	0.72 (0.42–1.24)	

NOTE: Occasional smokers are not included in the number of years smoked, pack-years, or years since quitting analyses.
Abbreviation: NA, could not be calculated.
[a]Adjusted for age, study site, BMI, education, family history of kidney cancer in a first-degree relative, and gender (years since quitting also adjusted for pack-years).
[b]For smoking history, this number represents the overall test of significance.

associations between RCCs and cigarette smoking by race. There are no previous published studies with which to compare our results for blacks. Our findings for white participants support those of several case–control studies in primarily white populations (15, 27, 28). A 2005 meta-analysis of 21 case–control and cohort studies mostly from North American and European populations reported an overall relative risk of 1.38 (95% CI, 1.27–1.50) for ever-smokers, using adjusted estimates (12). Recent findings from the Multiethnic Cohort study, which was 22.9% white and 16.3% black at baseline interview, report an approximately 2-fold increase in risk of RCCs associated with current cigarette smoking, but these findings were not stratified by race (14). On the basis of our findings, it does not appear that smoking contributes to the excess rates of RCCs seen in black Americans.

We had a sufficiently large sample to examine the effects of smoking stratified by hypertension and BMI, 2 variables that have been strongly associated with RCC and that vary in prevalence by race. Hypertension has been associated with RCCs in both men and women (9, 14, 29) and is more prevalent in the black population (30). Colt and colleagues observed a higher adjusted OR for hypertension and RCC in blacks (OR, 2.8; 95% CI, 2.1–3.8) than in whites (OR, 1.9; 95% CI, 1.5–2.4) in this study (21). In our study, when stratified by hypertension history, smoking remained a significant risk factor for RCC among normotensive white and black individuals but not among those who reported a prior diagnosis of hypertension. The only other study to concurrently examine smoking, hypertension, and RCC risk noted that risk of RCC was 2.49 times higher for hypertensive ever-smokers than for normotensive never smokers (relative risk, 2.49; 95% CI, 1.74–3.55), but estimates were not provided by race (14). When analyzing our data in the same manner, our findings are strikingly similar overall (OR, 2.49; 95% CI, 1.86–3.32, data not shown) and by race (OR, 2.38; 95% CI, 1.66–3.41 for whites and OR, 2.71; 95% CI, 1.65–4.45 for blacks, data not shown).

Our study found a significantly stronger effect of smoking among nonobese individuals. The association between obesity and RCCs has been consistently shown in both men and women of various racial/ethnic ancestries (14, 31–33), and obesity was more prevalent among blacks than among other racial groups (34). Smokers tend to have a lower BMI than nonsmokers, and smoking cessation is a risk factor for weight gain (35, 36). Among smokers in our study population, nonobese individuals are more likely to be current smokers ($P = 0.005$, data not shown). We have no explanation for the observed effect modification of smoking-related RCC risk by obesity and we cannot rule out the possibility of chance variation. Further investigations are necessary to confirm our findings.

Smoking cessation reduced the risk of RCCs for both whites and blacks compared with those who were current smokers, with a greater length of cessation offering the most benefit. The approximate 40% reduction in risk after 16 or more years of cessation reported here is similar to other studies of the same size (15, 27). A meta-analysis of 5 studies reported similar observations about smoking cessation and RCC risk, particularly among men (12). Two recent smaller studies that were not included in the meta-analysis have also confirmed RCC risk decreases as smoking cessation length increases (28, 37).

Our study has notable strengths, including a large population of black and white cases and controls, allowing for results to be presented by race. We also had detailed information on smoking and possible confounders. Coupled with BMI and history of hypertension, we were able to report on smoking-related risk of RCCs for specific subpopulations that have not been well-described, namely, normotensive and nonobese individuals.

Our study also had several limitations. Our ability to examine the complex interactions among the effects of race, smoking, hypertension, and obesity is limited by sample size, despite our relatively large study population.

Table 4. Adjusted ORs and 95% CIs for risk of RCC associated with smoking variables, by BMI and race

	White				Black			
	Cases	Controls	OR (95% CI)[a]	P_{trend}[a,b]	Cases	Controls	OR (95% CI)[a]	P_{trend}[a,b]
BMI < 30 kg/m²								
Number of years smoked				**<0.0001**				**0.005**
Never smoked	166	209	1.00 (ref)		54	110	1.00 (ref)	
≤9	37	50	0.99 (0.63–1.53)		4	19	0.30 (0.08–1.07)	
10–20	69	74	1.04 (0.71–1.54)		18	52	0.60 (0.27–1.31)	
21–30	49	65	0.83 (0.56–1.23)		31	48	1.24 (0.67–2.30)	
31–40	70	46	**1.70 (1.05–2.74)**		43	66	1.03 (0.58–1.82)	
41+	75	44	**2.09 (1.33–3.26)**		28	36	1.51 (0.76–3.03)	
Pack-years				**0.0002**				0.29
Never smoked	166	209	1.00 (ref)		54	110	1.00 (ref)	
0.1–≤10.99	60	82	0.94 (0.66–1.36)		34	69	0.80 (0.45–1.45)	
11–20.99	59	60	1.10 (0.69–1.75)		25	56	0.94 (0.50–1.79)	
21–40.99	81	79	1.15 (0.81–1.62)		36	58	0.94 (0.50–1.75)	
41+	100	57	**1.97 (1.31–2.95)**		28	38	1.21 (0.61–2.37)	
Years since quitting				0.09				**0.008**
Current	131	88	1.00 (ref)		73	110	1.00 (ref)	
<5	28	21	1.26 (0.63–2.54)		19	26	0.87 (0.40–1.85)	
6–15	38	32	0.94 (0.53–1.68)		13	29	0.55 (0.25–1.23)	
16–25	40	55	0.62 (0.35–1.08)		12	25	0.61 (0.26–1.46)	
25+	63	83	0.71 (0.42–1.21)		8	31	**0.29 (0.13–0.65)**	
Smoking history				0.06				0.23
Never smoked	166	209	1.00 (ref)		54	110	1.00 (ref)	
Occasional	16	22	1.00 (0.53–1.88)		14	17	1.67 (0.78–3.58)	
Former/light	99	117	1.04 (0.73–1.47)		24	68	0.58 (0.33–1.04)	
Current/light	20	25	0.94 (0.50–1.76)		35	57	1.34 (0.73–2.41)	
Former/heavy	70	73	1.11 (0.76–1.62)		28	43	0.84 (0.46–1.53)	
Current/heavy	111	63	**1.95 (1.25–3.03)**		36	53	1.13 (0.65–1.95)	
BMI of 30+ kg/m²								
Number of years smoked				0.15				0.76
Never smoked	140	77	1.00 (ref)		66	71	1.00 (ref)	
≤9	20	17	0.70 (0.31–1.62)		9	8	0.92 (0.30–2.82)	
10–20	38	29	0.75 (0.41–1.37)		21	15	1.47 (0.63–3.40)	
21–30	54	25	1.06 (0.61–1.85)		23	27	0.84 (0.40–1.74)	
31–40	58	27	1.06 (0.60–1.86)		26	20	1.55 (0.75–3.22)	
41+	39	22	0.90 (0.50–1.61)		11	13	0.88 (0.35–2.78)	
Pack-years				0.23				0.46
Never smoked	140	77	1.00 (ref)		66	71	1.00 (ref)	
0.1–≤10.99	35	27	0.71 (0.37–1.34)		29	22	1.58 (0.82–3.05)	
11–20.00	20	20	0.52 (0.26–1.04)		21	21	1.03 (0.49–2.13)	
20.01–40.00	80	29	1.40 (0.83–2.37)		26	25	1.32 (0.63–2.76)	
40.01+	74	43	0.79 (0.48–1.30)		14	15	1.07 (0.45–2.61)	
Years since quitting				0.21				0.68
Current	77	35	1.00 (ref)		37	30	1.00 (ref)	
<5	23	10	1.59 (0.68–3.70)		9	9	1.25 (0.41–3.82)	
6–15	49	28	0.82 (0.41–1.62)		21	19	1.19 (0.53–2.68)	
16–25	36	28	0.66 (0.30–1.48)		13	15	1.22 (0.33–4.49)	
25+	25	19	0.61 (0.24–1.54)		10	11	1.27 (0.32–5.00)	
Smoking history				0.18				0.50
Never smoked	140	77	1.00 (ref)		66	71	1.00 (ref)	
Occasional	16	3	3.05 (0.69–13.5)		6	13	0.40 (0.14–1.13)	

(Continued on the following page)

Table 4. Adjusted ORs and 95% CIs for risk of RCC associated with smoking variables, by BMI and race (Cont'd)

	White				Black			
	Cases	Controls	OR (95% CI)[a]	P_{trend}[a,b]	Cases	Controls	OR (95% CI)[a]	P_{trend}[a,b]
Former/light	41	40	0.57 (0.33–1.01)		30	32	1.06 (0.56–2.01)	
Current/light	14	7	1.21 (0.44–3.29)		20	15	1.20 (0.53–2.75)	
Former/heavy	92	44	1.16 (0.72–1.86)		23	22	1.47 (0.67–3.20)	
Current/heavy	62	28	1.01 (0.56–1.81)		17	14	0.88 (0.38–2.01)	

NOTE: Occasional smokers are not included in number of years smoked, pack-years, or years since quitting analyses.
[a]Adjusted for age, study site, hypertension, education, family history of kidney cancer in a first-degree relative, and gender (years since quitting also adjusted for pack-years).
[b]For smoking history, this number represents the overall test of significance.

The response rates were low, similar to other recent population-based case–control studies, but the nonresponse adjustment helped to minimize the potential bias. In addition, height, weight, and hypertension status were obtained by self-report, which may result in misclassification. If misclassification was similar between cases and controls, it would bias our findings toward the null. If it differed, our measures of effect may be over- or underestimated. Similarly, if misclassification of exposures differed by racial group, comparisons across race may not be accurate. There may also be differences in residual confounding between white and black participants, which could also affect comparisons by racial group. We were also unable to obtain information on specific cigarette usage patterns for 3.8% of our white subjects and 5.8% of our black subjects who reported occasional cigarette smoking. Thus, these individuals are not included in calculations requiring number of cigarettes a day or years of smoking. Finally, differences in sample size alter the power to detect associations in certain subgroups examined in these analyses. Some subgroups had small numbers of individuals and results should be interpreted with caution. However, as RCC is relatively rare, case–control studies are the best available tool to address the complex etiology of this disease.

In conclusion, this study confirmed previous reports of an association between cigarette smoking and RCCs among whites and is the first to report a potential increased risk of RCC among black smokers. Smoking cessation decreased risk of RCCs among both whites and blacks. Our results, which suggest cigarette smoking is an important risk factor, particularly among nonobese individuals and those with no history of hypertension, are intriguing and should be confirmed in other populations.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interests were disclosed.

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