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HYPERTENSION AND OBESITY AND THE RISK OF KIDNEY CANCER IN TWO LARGE COHORTS OF US MEN AND WOMEN

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Abstract

Kidney cancer incidence is increasing globally. Reasons for this rise are unclear, but could relate to obesity and hypertension. We analyzed longitudinal relationships between hypertension and obesity and kidney cancer incidence in 156,774 participants of the Women's Health Initiative (WHI) clinical trials and observational studies over 10.8 years. In addition, we examined the impact of blood pressure (BP) on kidney cancer deaths over 25 years among the 353,340 men screened for the Multiple Risk Factor Intervention Trial (MRFIT). In the WHI, systolic SBP was categorized in 6 groups from <120 to >160 mmHg and body mass index (BMI) was categorized using standard criteria. In age-adjusted analyses, kidney cancer risk increased across SBP categories (p-value for trend <0.0001) and BMI categories (p-value for trend <0.0001). In adjusted Cox proportional hazards models, both SBP levels and BMI were predictors of kidney cancer. In the MRFIT sample, there were 906 deaths after an average of 25 years of follow-up attributed to kidney cancer amongst the 353,340 participants aged 35–57 years at screening. The risk of death from kidney cancer increased in a dose-response fashion with increasing SBP (HR=1.87 for SBP>160 versus <120 mmHg; 95% CI, 1.38–2.53). Risk was increased among cigarette smokers. Further research is needed to determine the pathophysiologic basis of relationships between both

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higher BP and the risk of kidney cancer, and whether specific drug therapies for hypertension can reduce kidney cancer risk.

Keywords

blood pressure; body weight; epidemiology; kidney neoplasms; obesity; women's health

Introduction

The incidence of kidney cancer is increasing throughout the world amongst all age groups, races, and for all tumor sizes.(1,2) Metastatic kidney cancer is one of the most treatment-resistant malignancies with a five-year relative survival rate of 12.3% at time of diagnosis. (3)

Risk factors for kidney cancer include hypertension, increased body weight, and smoking. (4–8) Hypertension has been found to increase risk for kidney cancer in numerous prospective studies. (9–12) However, the duration of follow-up for many of these studies is short. Several studies have lacked measured blood pressure (BP) values.(13,14) The few studies that have included data on women reported increased risk of kidney cancer with higher levels of BP.(2,9,10,15) We previously reported a positive association between BP levels and kidney cancer in men over 16 years in the Multiple Risk Factor Intervention Trial (MRFIT).(16)

Excess body weight has also been recognized as a risk factor for kidney cancer in general, and specifically in women,(2, 17–19) with overweight or obesity estimated to be causally related to over 25% of US kidney cancer cases.(5,18)

Furthermore, few studies have examined obesity and hypertension together as risk factors for kidney cancer. Obesity is a risk factor for hypertension, thus they may represent a shared causal mechanism.(2) One prospective US study identified a relative risk of 2.82 (95% CI: 1.97, 4.02) for all kidney cancer cases in individuals who were both hypertensive and obese, compared with their lean normotensive counterparts.(2) Another analysis, which simultaneously stratified by body mass index (BMI) and BP categories, found that BMI showed only a non-significant effect on renal cell carcinoma (RCC) incidence when BP was markedly elevated.(10)

We examined the relationship between levels of hypertension and degree of obesity as risk factors for kidney cancer both separately and in relationship to one another over 10.8 years in a large racially diverse female population. We complemented these analyses with an evaluation of the long-term associations between BP, cigarette smoking and kidney cancer specific mortality in men, examining 25 years of follow-up in the 353,340 men screened for the MRFIT.(20)

The Women's Health Initiative (WHI) (21,22) and MRFIT (20) are the two largest studies of the relationship of BP levels to risk of kidney cancer that include both the actual measurements of BP and long term follow up to account, in part, for the incubation period

from BP measurement to development of kidney cancer. The WHI provides more detailed information on measures such as obesity, BMI, waist circumference (WC), drug therapy and risk of kidney cancer. The MRFIT includes a larger sample of cigarette smokers and longer term follow up to kidney cancer.

Methods

Study Populations

The WHI Observational Study (WHI-OS) and WHI Clinical Trial (WHI-CT) studies conducted recruitment across 40 US clinical centers, enrolling a combined total of 161,856 women aged 50 to 79 years from September 1993 to December 1998. Concentrated efforts were made to enroll a racially and ethnically diverse sample. All participants underwent a baseline physical exam and longitudinal follow-up with scheduled exams and questionnaire completion, as detailed in prior publications. (21,22) The WHI provides detailed information on BMI, waist circumference (WC), drug therapy and development of kidney cancer.

MRFIT methods have been described previously. (20) The MRFIT screened 361,662 men aged 35–57 at 22 clinical centers throughout the United States between 1973–1975.(34) Information recorded from each participant included date of birth, social security number, race, cigarette smoking status, use of medication for diabetes and history of hospitalization for myocardial infarction. All participants of each study signed consent forms for participation, which were approved by the institutional review boards of collaborating institutions.

Inclusion Criteria & Measurements-WHI

We included women of the WHI-CT and WHI-OS with baseline height and weight measurements and self-reported race/ethnicity. We excluded women with a baseline BMI <18.5 kg/m^2 (n=1,383) as this group may include women with low BMI due to other health conditions. Race/ethnicity was categorized according to baseline self-report. A prior diagnosis of diabetes mellitus, diagnosis and treatment of hypertension, and current smoking status were self-reported. Height, weight, WC and BP levels were assessed during baseline WHI examinations. Kidney cancer was assessed from baseline to August 2009. Cancer diagnoses were ascertained through questionnaire responses and review of medical records that were locally (n=318) or centrally (n=97) adjudicated.

Analyses of hypertension, body weight and kidney cancer incidence - WHI

We used descriptive statistics to examine the distribution of race/ethnicity, BP, BMI and WC, smoking status and diabetes prevalence at baseline among women with and without incident kidney cancer. In unadjusted analyses, we assessed for trends of cancer incidence across categories of BP, BMI and WC.

Cox proportional hazards modeling assessed whether SBP and BMI categories were independently associated with development of incident kidney cancer after adjusting for age, smoking status, race/ethnicity and diabetes mellitus at baseline. The same analyses were

repeated substituting DBP for SBP. We then used a similar modeling approach to determine how hypertension and central obesity (WC categories) influenced kidney cancer risk.

Inclusion Criteria & Measurements – MRFIT

For the MRFIT analyses, we include data from screened participants with measured baseline BP values (n=353,340). They included date of birth, social security number, serum cholesterol, race, cigarette smoking status, and use of medication for diabetes and history of hospitalization for myocardial infarction. The average of the second and third BP readings, measured with a standard mercury sphyngomanometer, was categorized into 5 mm (diastolic) and 10 mm (systolic) increments, as well as clinical hypertension categories. No information is available regarding obesity or the use of antihypertensive medications in the MRFIT sample.

Analyses of blood pressure and kidney cancer deaths in men in MRFIT

We used Cox proportional hazards modeling with stratification by clinical center to determine the risk of mortality from kidney cancer related to BP categories. We report unadjusted hazard ratios (HRs) and HRs adjusted for age, serum cholesterol, cigarette use, race (black versus non-black), and diabetes status.

Because there is a known strong association between kidney cancer and end stage renal disease (ESRD),(23) and hypertensive kidney damage is hypothesized to be a mechanism by which elevated BP increases renal cancer risk,(24,25) we also utilized information obtained by matching data for MRFIT participants with the national registry of treated cases of ESRD of the Centers for Medicare & Medicaid Services.(25) With this information we were able to determine how many participants had ESRD prior to dying from kidney cancer.

The vital status of each participant enrolled in the MRFIT cohort was determined through 1999 by utilizing the National Death Index and records from the Social Security Administration. Death certificates from respective departments of health were obtained and the cause of death determined by a qualified nosologist.(26) For the purposes of this study, kidney cancer is defined as a primary malignancy of the kidney, renal pelvis, or ureter (ICD-9 code 189 and ICD-10 codes C64, C65, and C66).

All analyses were completed using SAS version 9.1 (SAS Institute, Cary, NC). For all results, a significant finding was defined by a p-value of <0.05.

Results

Analyses of kidney cancer incidence in women

A total of 156,774 women were eligible for inclusion in these analyses from the WHI-CT and WHI-OS samples. Baseline characteristics revealed a racially/ethnically diverse population with over a third of participants reporting a history of hypertension, nearly 70% overweight or obese and less than 10% reporting a history of diabetes or current smoking. (Table 1) During the average 15 years follow-up, 407 incident kidney cancers occurred. In unadjusted analyses for trend, kidney cancer incidence significantly increased with higher

SBP and DBP, prior hypertension diagnosis and/or treatment, and higher BMI or WC categories.

All SBP categories ≥140 mmHg, i.e. women with systolic hypertension, showed higher point estimates of kidney cancer risk, compared to SBP levels of ≤ 120 mmHg. Women with SBP of 120.1–130.0 mmHg also had a significant (HR 1.33, 1.01–1.75) increase in kidney cancer incidence, compared with those who had SBP ≤120. (Table 2) Elevated DBP (≥90 mmHg; HR 1.56, 1.06–2.29) and BMI were independently associated with kidney cancer. In addition, risk of kidney cancer increased with increasing age, SBP, BMI and cigarette smoking.

In analyses stratified by BMI categories after adjustment for age, smoking, race/ethnicity, there was an increased risk of kidney cancer associated with elevated SBP in each strata of BMI, although consistently significant only for women with a BMI ≥30. (Table 3) This was likely due, in part, to the small number of women with elevated BP and normal (<25 kg/m^2) or overweight (25.0–29.9 kg/m^2) BMI. Among obese women, increasing SBP showed a dose response association with kidney cancer risk, with women in the highest BP category (≥160 mmHg) having a HR of 1.94 (1.07–3.50). A similar pattern was found when categorical DBP was modeled within each BMI category.

Applying the same modeling strategy with WC quartiles instead of BMI categories, the point estimates of kidney cancer risk generally increased with WC, with risk almost doubling (HR 1.91, 1.38–2.63) for women in the highest WC category (>97.9cm). Both elevated SBP and DBP remained significant predictors of kidney cancer in models that included WC. (Supplemental Table 1)

The rate of women developing kidney cancer was higher for women on treatment for hypertension, varying from 2.2/1,000 person-years (PYs) for no hypertension to 3.6/1,000 PYs for women on antihypertensive drug therapy. In general, among women treated for hypertension, the percentage developing kidney cancer increased with their SBP levels, especially at the extremes. There were very few women with elevated BP (SBP >140 mmHg) but no drug therapy who developed kidney cancer. Within each BP category, there was generally a higher risk of kidney cancer among women treated as compared to not treated but the number of kidney cancers is relatively small within any single SBP category. (Supplemental Table 2)

Analyses of kidney cancer mortality in men

During the 25 years of follow-up in MRFIT, 906 deaths from kidney cancer were identified (0.26% of participants) with 840 of the deaths among white men (0.26%), 46 deaths were among black men (0.20%), and 20 deaths were among men of other races (0.16%).

On average, men who died from kidney cancer had greater SBP at entry (133.0 mmHg) compared to those who did not (130.0 mmHg). The percent dying of kidney cancer increased with higher BP levels even throughout the normotensive range.(Table 4) Compared to men with SBP <120 mmHg, the adjusted HRs ranged from 1.29 for those with

SBP of 120–129 mmHg to 1.87 for participants with SBP >160 mmHg. The adjusted HR corresponding to a one SD higher SBP level was 1.18 ($p<0.0001$).

The relationship between baseline DBP and mortality from kidney cancer was weaker than for SBP.(Table 4) The adjusted HRs ranged from 1.16 to 1.49 and did not increase in a graded manner. Average levels of DBP for those who died from kidney cancer and those who did not were 84.9 and 83.8 mmHg. The adjusted HR for DBP corresponding to a one SD higher level was 1.13 ($p<0.0001$). For comparison, the corresponding HRs for CVD and all cancers are 1.38 ($p<0.0001$) and 1.06 ($p<0.0001$).

After 10 years, the cumulative percent dying in the 1st (<117 mmHg) and 5th (>141 mmHg) quintiles were 0.043% and 0.086%. After 25 years, these percents were 0.20% and 0.40%. The adjusted HR for death from kidney cancer for the upper versus lower quintile of SBP was 1.73 (95% CI: 1.38–2.16; $p<0.0001$).

Among participants who died from kidney cancer, 45.5% reported smoking cigarettes at entry as compared to 36.4% for men who did not die from kidney cancer. The adjusted HR for death from kidney cancer associated with smoking was 1.75 (95% CI: 1.53–2.00; $p<0.0001$). The effects of smoking and SBP on risk of death from kidney cancer were additive. Risk was lowest among non-smokers with SBP <120 mmHg and highest among smokers with SBP >120 mmHg. HR comparing nonsmokers with SBP <120 mmHg to smokers with SBP >140 mmHg was 2.68.(Table 5)

Covariates not associated with risk of kidney cancer specific mortality in the Cox model included: black race (adjusted HR=0.75; 95% CI: 0.56–1.02), serum cholesterol (adjusted HR per 40 mg/dl higher level = 1.01; 95% CI: 0.94–1.08), and use of medication for diabetes (adjusted HR=1.15; 95 %CI: 0.69–1.92).

Only 19 MRFIT participants who died of kidney cancer (2.1%) were identified in the ESRD registry as compared to 1.2% of those who did not die from kidney cancer entered the registry. For the 19 participants, the average length of time from entering the ESRD registry to kidney cancer death was 2.5 years; average SBP and DBP at entry were 140 and 89 mmHg. None had a history of diabetes and the average age at screening was 45.5 years.

Discussion

We observed an excess risk of kidney cancer in both men and women with increasing BP levels. These relationships were independent of the association of kidney cancer with elevated body weight (measured by either BMI or WC), or cigarette smoking.

The results of both the MRFIT and WHI are consistent with the prior literature. While a recent study did not find an independent risk of hypertension and kidney cancer,(27) the study evaluated a single BP measurement in late adolescence (age 17) at the time of recruitment for military service. Over 900,000 recruits were followed up over 14 years, linked to the Israeli Cancer Registry. The relative risk of kidney cancer was 1.28 (0.17–9.50) among 4,223 recruits with established hypertension by age 17. This is consistent with the HR of 1.18 in the MRFIT sample for a 1 SD increase in SBP. It would be important to

determine whether the known increase in BP from adolescence to adult age is a risk factor for kidney cancer and whether independent of weight gain.

Obesity and hypertension, to some extent, may represent a shared causal mechanism in the development of kidney cancer. Obesity is associated with increased glomerular filtration rate and increased renal plasma flow, which may render the kidney more susceptible to kidney damage and carcinogenesis.(24,28) Furthermore, patients with hypertension suffer chronic renal hypoxia caused by the up-regulation of hypoxia-inducible factors that may in turn play a role in oncogenesis.(10,29) Both obesity and hypertension have also been associated with oxidative stress (30) and lipid peroxidation,(24,31) which is hypothesized to play a role in kidney cancer etiology. In addition, obesity could increase cancer risk through increased levels of insulin and insulin-like growth factor I. (32–34) Sporadic clear-cell kidney cancer commonly involves mutations in the *von Hippel-Lindau* (VHL) tumor suppressor gene; with as many as 91% of clear cell kidney cancers containing an alteration in the VHL gene. (35) The VHL gene is an important regulator of hypoxia inducible factors, fibronectin assembly, and overall cell cycle regulation.

Chronic kidney disease could represent a likely alternative explanation for associations between BP and kidney cancer.(25) Chronic kidney disease secondary to elevated BP is an important risk factor for kidney cancer.(23,25) Subclinical kidney damage secondary to elevated BP may be in the pathway from elevated BP to kidney cancer. Alternatively, environmental agents may contribute to both kidney injury (leading to cancer onset) and elevated BP. These studies do not prove a causal association of elevated BP and kidney cancer.

For all women combined, we found higher rates of kidney cancer among women with treated (versus untreated) hypertension and slightly lower point estimates of kidney cancer incidence among those without hypertension. In addition, within blood pressure strata, point estimates for kidney cancer incidence were typically lower for pharmacologically treated, versus untreated individuals. These findings potentially suggest that anti-hypertensive medications may contribute to kidney cancer risk. However, severity or duration of hypertension alone could explain such findings. For example, women whose elevated blood pressure is not treated pharmacologically are more likely to have mild hypertension controlled with lifestyle alone, or hypertension of shorter duration (e.g., recently diagnosed and attempting lifestyle change prior to initiation of drug therapy) compared with those who are prescribed anti-hypertensive medications. Adjusting for the presence of hypertension has eliminated excess risk associated with pharmacotheraphy in multiple studies.(24,36) Furthermore, one large study found that antihypertensive use did not modify the relationship between blood pressure and kidney cancer incidence, while among individuals taking antihypertensive drugs, only those with poorly controlled blood pressure showed a significantly increased cancer risk.(10) As a result, studies have typically concluded that associations between antihypertensive medication and kidney cancer are unlikely to be causal, reflecting instead confounding by the presence of hypertension.(1,22,24,37)

Further prospective studies are needed to determine whether treatment and control of hypertension can reduce the risk of kidney cancer and if so, whether specific drug therapies

would differ in preventive efficacy. The low incidence of kidney cancer precludes the use of data from any specific prior hypertension trial to answer this question. However, it is possible that pooling the results from many large clinical trials may provide a clue as to whether BP lowering reduces kidney cancer risk. It is possible that combination of hypertension and/or obesity, renal damage and host, genetic markers could identify a very high risk of kidney cancer and lead to specific treatment strategies.

This study has several limitations, which are in part addressed by the use of two complementary samples. As cancer development occurs over prolonged periods of time, 15–25 years may still be a short duration of follow-up time. The WHI sample comprises an ethnically diverse population, however, a relatively low number of incident kidney cancer occurred in ethnic groups other than white women precluding evaluation of ethnic-specific patterns. A similar problem was found for MRFIT in which almost all cases occurred in white men. The geographic and ethnic diversity of the samples add an important element of external validity to the literature on kidney cancer. Only a single measurement of risk factors was obtained for the men screened for MRFIT. Results from WHI used only baseline measurement of BP. Experimental studies that evaluate effects of change in BP on risk of kidney cancer would prove further evidence of possible role of hypertension in the etiology of kidney cancer. We are unable to evaluate the association between hypertension or obesity and specific subtypes of kidney cancer from these data. However, as over 85% of kidney cancers arise from the renal parenchyma (1) it is likely that the outcomes assessed here primarily reflect renal cell carcinoma.

Perspectives

We found that obesity and hypertension were independently associated with the development of kidney cancer, and that hypertension shows a robust association with kidney cancer in long-term follow-up in US men and women. The mechanisms of these associations are not known, nor are the role of specific antihypertensive drug therapy in reducing kidney cancer risk.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Novelty and Significance

What Is New

Prior research on obesity, hypertension and kidney cancer has been limited by small sample sizes (15) and self-reported predictors (2,15,16). Furthermore, of the prospective studies we identified with mixed-sex or female samples (2,7–9,16) only two measured blood pressure.(9,17) Both of these studies are European, thus their findings may not generalize to the more racially/ethnically diverse US population. The current study examines the relationship between levels of hypertension and degree of obesity as risk factors for kidney cancer both separately and in relationship to one another over a prolonged period of time in a large racially diverse female population. It also analyzes the association between blood pressure and kidney cancer deaths over 25 years of follow-up in men.

What Is Relevant

An understanding of the etiology of kidney cancer is essential for developing better preventive measures in this era of escalating incidence.

Summary

Among 156,774 participants of the WHI, blood pressure and BMI were independent predictors of kidney cancer incidence in adjusted models. MRFIT data showed that the risk of death from kidney cancer increased in a dose-response fashion with increasing blood pressure, over an average of 25 years of follow-up. In addition, smoking and systolic blood pressure were independently associated with increased on risk of death from kidney cancer.

Table 1

WHI Baseline Sample Description for the Sample, and By Kidney Cancer Diagnosis Status

Data are presented as frequency (column percent) for the whole sample and frequency (row percent) for subsamples.

Measures		Whole Sample (N=156,774)	Without Kidney Cancer (N=156,367)	With Kidney Cancer (N=407)	p-value	Trend p-value	Age-adjusted p-value	Age-adjusted trend p-value
		N (% of population)		N (%)				
Race and Ethnicity	Native American	695 (0.44)	692	3 (0.43)	0.485		0.605	
	Asian	4,022 (2.57)	4,015	7 (0.17)				
	African American	14,411 (9.19)	14,379	32 (0.22)				
	Hispanic	6,414 (4.09)	6,400	14 (0.22)				
	White	131,232 (83.71)	130,881	351 (0.27)				
Systolic BP (mmHg)	≤120	60,098 (38.35)	59,985	113 (0.19)	<.0001	<.0001	0.0003	0.003
	120.1 –130	35,727 (22.80)	35,630	97 (0.27)				
	130.1 – 140	28,436 (18.15)	28,362	74 (0.26)				
	140.1 – 150	16,836 (10.74)	16,766	70 (0.42)				
	150.1 – 160	8,880 (5.67)	8,851	29 (0.33)				
	> 160	6,730 (4.29)	6,707	23 (0.34)				
Diastolic BP (mmHg)	<90	149,557 (95.45)	149,179	378 (0.25)	0.023	0.031	0.017	0.017
	≥90	7,124 (4.55)	7,096	28 (0.39)				
Hypertension Diagnoses	None	97,722 (65.9)	97,507	215 (0.22)	<.0001	<.0001	0.0002	0.021
	Untreated	12,022 (8.11)	11,992	30 (0.25)				
	Treated	38,535 (25.99)	38,395	140 (0.36)				
BMI (kg/m^2)	18.5 – 24.9	54,248 (34.60)	54,140	108 (0.20)	0.003	<.0001	<0.0001	<0.0001
	25.0 – 29.9	54,876 (35.00)	54,732	144 (0.26)				
	30.0 – 34.9	29,298 (18.69)	29,215	83 (0.28)				
	35.0 – 39.9	12,017 (7.67)	11,972	45 (0.37)				
	≥40	6,335 (4.04)	6,308	27 (0.43)				
Waist Circumference (cm)	≤75	30,641 (19.60)	30,583	58 (0.19)	<.0001	<.0001	<0.0001	0.002
	75 – 81.2	31,943 (20.43)	31,878	65 (0.20)				
	81.3 – 88.1	31,179 (19.94)	31,107	72 (0.23)				
	88.2 – 97.9	31,231 (19.98)	31,140	91 (0.29)				

Measures		Whole Sample (N=156,774)	Without Kidney Cancer (N=156,367)	With Kidney Cancer (N=407)	p-value	Trend p-value	Age-adjusted p-value	Age-adjusted trend p-value
	>97.9	31,341 (20.05)	31,221	120 (0.38)				
Smoking at baseline	Never	78,833 (50.95)	78,642	191 (0.24)	0.167	0.076	0.085	0.030
	Past	65,220 (42.15)	65,045	175 (0.27)				
	Current	10,678 (6.90)	10,642	36 (0.34)				
Diabetes at baseline	No	147,350 (94.04)	146,970	380 (0.26)	0.564	0.564		0.669
	Yes	9,334 (5.96)	9307	27 (0.29)				

Table 2

Cox Regression of Kidney Cancer Incidence With Models Combining BMI and BP Categories in WHI

SBP and DBP are modeled separately. Each model is adjusted for race/ethnicity in addition to the variables in the table.

Variables		HR (95% CI)
Model examining systolic blood pressure		
Age		1.03 (1.01, 1.04)
BMI (kg/m^2)		
	18.5–24.9	1.00
	25–29.9	1.28 (1, 1.65)
	30–34.9	1.39 (1.04, 1.86)
	35–39.9	1.79 (1.24, 2.58)
	≥40.0	2.30 (1.49, 3.54)
Smoking		1.62 (1.15, 2.28)
Systolic BP (mmHg)		
	≤120.0	1.00
	120.1–130.0	1.33 (1.01, 1.75)
	130.1–140.0	1.24 (0.92, 1.67)
	140.1–150.0	1.93 (1.42, 2.63)
	150.1–160.0	1.48 (0.97, 2.26)
	>160.0	1.54 (0.96, 2.45)
Diabetes		0.97 (0.65–1.45)
Model examining diastolic blood pressure		
Age		1.04 (1.02, 1.05)
BMI (kg/m^2)		
	18.0–24.9	1.00
	25.0–29.9	1.32 (1.03, 1.7)
	30.0–34.9	1.47 (1.1, 1.96)
	35.0–39.9	1.91 (1.33, 2.75)
	≥40.0	2.48 (1.61, 3.80)
Smoking		1.60 (1.13, 2.26)
Diastolic BP (mmHg)		
	≤90.0	1.00
	>90.0	1.56 (1.06, 2.29)
Diabetes		1.01 (0.68, 1.51)

Table 3

HRs and 95% CIs for Kidney Cancer Incidence for Different Categories of BP, Modeled Within BMI Strata in WHI

Models are adjusted for age, smoking and race/ethnicity.

BMI (kg/m^2)	Blood Pressure (mmHg)	Individuals at risk (number)	Cancer cases (number)	% that developed cancer	HR (95% CI)
Models examining SBP					
BMI <25	SBP <140	44,284	84	0.19	1.00
	SBP 140–159	7,712	18	0.23	1.12 (0.67, 1.89)
	SBP ≥160	2,218	6	0.27	1.25 (0.54, 2.91)
BMI 25.0–29.9	SBP <140	42,007	98	0.23	1.00
	SBP 140–159	10,054	42	0.42	1.66 (1.14, 2.40)
	SBP ≥160	2,798	4	0.14	0.55 (0.20, 1.49)
BMI ≥30	SBP <140	34,027	91	0.27	1.00
	SBP 140–159	10,880	49	0.45	1.67 (1.17, 2.38)
	SBP ≥160	2,727	14	0.51	1.94 (1.07, 3.50)
Models examining DBP					
BMI <25	DBP <90	51,657	101	0.20	1.00
	DBP ≥90	2,551	7	0.27	1.47 (0.68, 3.17)
BMI 25.0–29.9	DBP <90	51,172	137	0.27	1.00
	DBP ≥90	3,675	7	0.19	0.76 (0.36, 1.63)
BMI ≥30	DBP <90	43,193	132	0.31	1.00
	DBP ≥90	4,433	22	0.50	1.75 (1.11, 2.76)

Table 4

Relationship between Baseline BP and Mortality from Kidney Cancer Over an Average Follow-up of 25 Years in the MRFIT Cohort.

Baseline	Number of Men	Deaths from Kidney Cancer		Unadjusted HR (95% CI)	Adjusted HR* (95% CI)
		N	%		
SBP (mmHg)					
<120	88,641	165	0.19	1.00	1.00
120–129	100,168	241	0.24	1.33 (1.09–1.62)	1.29 (1.06–1.58)
130–139	80,582	233	0.29	1.64 (1.34–2.01)	1.52 (1.25–1.86)
140–149	45,171	129	0.29	1.69 (1.34–2.13)	1.48 (1.17–1.86)
150–159	21,889	78	0.36	2.22 (1.69–2.91)	1.82 (1.39–2.40)
>160	16,889	60	0.36	2.41 (1.79–3.25)	1.87 (1.38–2.53)
DBP (mmHg)					
<80	118,857	255	0.21	1.00	1.00
80–84	79,312	198	0.25	1.18 (0.98–1.43)	1.16 (0.97–1.40)
85–89	58,358	175	0.30	1.44 (1.19–1.75)	1.41 (1.16–1.71)
90–94	46,541	147	0.32	1.55 (1.27–1.90)	1.49 (1.21–1.83)
95–99	24,716	61	0.25	1.24 (0.94–1.64)	1.19 (0.90–1.58)
≥100	25,556	70	0.27	1.46 (1.12–1.91)	1.39 (1.06–1.81)

Table 5

Risk of Death from Kidney Cancer According Smoking Status and SBP Relative to Non-Smoking with Systolic Blood Pressure < 120 mmHg in the MRFIT cohort.

Smoker	SBP Level (mmHg)	Number of Participants	No Kidney Cancer Deaths	No Kidney Cancer %	Adjusted HR	95% CI	P-value
No	< 120	56,899	84	0.15	1.00	Ref.	
No	120–139	114,808	248	0.22	1.43	1.12–1.84	0.005
No	≥140	52,999	163	0.31	1.92	1.47–2.50	<0.0001
Yes	< 120	31,742	81	0.26	2.00	1.48–2.72	<0.0001
Yes	120–139	65,942	226	0.34	2.71	2.10–3.48	<0.0001
Yes	≥140	30,950	104	0.34	2.68	2.00–3.58	<0.0001