BODY MASS INDEX AND OTHER RISK FACTORS FOR KIDNEY CANCER IN MEN: A COHORT STUDY IN LITHUANIA

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SUMMARY

Objectives: Previous studies have observed notable unexplained geographic differences in incidence of kidney cancer in Europe. Lithuania is among the countries with the highest incidence and mortality. Our objective was to investigate the effect of different lifestyle, anthropometric and biological factors on the risk of kidney cancer in Lithuanian men.

Methods: This population-based cohort study included 6,849 men initially free from cancer. During the follow-up (1978–2008), 79 incident cases of kidney cancer were identified. Cox proportional hazards regression models were used to estimate hazard ratios (HR) and corresponding 95% confidence intervals (95% CI).

Results: Risk of kidney cancer was significantly associated with increasing body mass index (BMI), the adjusted HR for ≥ 35 vs. < 25 kg/m^2 was 3.00, 95% CI 1.10–8.19 and the HR per 1 unit increment of BMI was 1.07, 95% CI 1.01–1.14. In overweight men (BMI ≥ 25 kg/m^2), the HRs for kidney cancer per 10 mmHg increment of systolic or diastolic blood pressure were 1.10, 95% CI 0.96–1.25 and 1.26, 95% CI 1.01–1.56, respectively. We found no significant association between smoking, alcohol consumption or total serum cholesterol level and kidney cancer risk.

Conclusions: This study supports a link between increased BMI and the development of kidney cancer among men in Lithuania. Hypertension appears to be associated with risk of kidney cancer in overweight men, although the assessment was limited by the lack of statistical power.

Key words: kidney cancer, hypertension, body mass index, risk factors, cohort study

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INTRODUCTION

Kidney cancer is a common type of urologic tumours. Among men in Europe it ranks 5th in the list of cancer incidence and accounts for 4% of all malignancies (4th and 6%, respectively, in Lithuania) (1). Kidney cancer rates have been increasing in recent decades in most European countries and in the United States, although stabilisation of mortality trends has been achieved in many highly developed countries (2–4). Lithuania with 20.2 per 100,000 person-years is the country with the 5th highest incidence rate of kidney cancer among men in the world (1, 2). High incidence rates were also estimated in Belarus (24.0 per 100,000 person-years), Estonia (21.3 per 100,000 person-years), Latvia (20.7 per 100,000 person-years), and the Czech Republic (20.7 per 100,000 person-years) (1). Relatively low rates are observed in the Southern and Southeastern European countries, as well as in Africa and Southern Asia (1, 2).

Most of the increases in kidney cancer since the 1980s have occurred in early stage tumours and rising incidence rates are partly attributable to improvements in diagnostic imaging (3). International variations in rates and time trends suggest that environmental factors are likely to play a role in the aetiology of kidney cancer. The International Agency for Research on Cancer Working Group of Experts concluded that there is sufficient evidence for a causal relationship between tobacco smoking and kidney cancer (5), although the risk associated with cigarette smoking is relatively modest (6). Previous studies and evaluations found inverse dose-response relationship or no effect for alcohol consumption and risk of kidney cancer (5, 7–9). Metabolic factors (6, 10, 11), including overweight and obesity (9–17) or elevated blood pressure (9, 10, 14, 16) have been established as causes of kidney cancer. It has been hypothesized that glucose and triglycerides (10, 18), cholesterol level (19, 20) or adult attained height (9, 15) may increase the risk of developing kidney cancer; however, the evidence of the relationship has been limited and inconsistent. The risk factors for kidney cancer have been exclusively documented for developed countries (4). According to Li et al., there is no information on any genetic, lifestyle, or environmental factors that could explain notable regional differences in kidney cancer incidence rates in Europe (2). Therefore, the identification of modifiable risk factors in high risk population of Central and Eastern Europe is important, as it may offer an opportunity for the primary prevention of kidney cancer.

In this study, we investigated the association between body mass index (BMI), blood pressure, as well as smoking, alcohol consumption and total serum cholesterol (TSC) level, and the risk

of kidney cancer using data collected in two population-based cohort studies with up to 30 years of follow-up.

MATERIALS AND METHODS

Study Population and Cancer Follow-up

Two cohorts – the Kaunas Rotterdam Intervention Study (KRIS) and the Multifactorial Ischaemic Heart Disease Prevention Study (MIHDPS) – are included. The KRIS is a WHO-coordinated prospective cohort study of a random sample of 2,447 men aged 45–59, living in the city of Kaunas, Lithuania, who were recruited during the years 1972–1974. The MIHDPS was carried out in 1977–1980 among 5,933 Kaunas men, aged 40–59. More detailed information about the study has been published elsewhere (21).

In all, 8,380 participants were available for analysis. During the follow-up period, the vital status of the subjects was determined from the Lithuanian Residents' Register Service. In addition, dates and causes of death were confirmed from death certificates at the Archives Department under the government of the Republic of Lithuania. We excluded 1,531 men because of duplicates (n = 469), unknown vital status at the end of follow-up (n = 389), death or diagnosis of cancer before the start of the follow-up (n = 309), and missing data for any of the covariates (n = 364). The final number of participants included in the study was 6,849.

Follow-up time started on 1 January 1978 or, to avoid the influence of subclinical disease, 3 years after the date of interview (whichever came later). We identified cases of kidney cancer from the Lithuanian Cancer Registry, which has population-based information available since 1978. In addition, deaths from kidney cancer (2 cases) were identified in the National Archive on Causes of Death. For the present study, the kidney cancer codes were C64.0 (189.0) of the International Statistical Classification of Diseases, Injury and Causes of Death, 10th (9th) Revision.

Person-years were calculated until the day when participants were diagnosed with cancer or died, or were lost to follow-up, or censored at 31 December 2008, whichever came first.

Ethical approval for this study was obtained from the Regional Biomedical Research Ethical Committee in Vilnius (No. 158200-02-280-65).

Assessment of Exposure

Data were collected using a standard protocol and uniform methods of measurement. At baseline, all participants underwent physical examination (height, weight, blood pressure, and TSC). Height (cm) and weight (kg) were measured in light clothing and without shoes by using a bodymeter and stadiometer, respectively, by registered nursing staff. TSC levels were measured in serum using an enzymatic (CHOD-PAP) method (22). An interview was used to collect information on demographic factors, smoking and drinking habits as well as antihypertensive or lipid-lowering medication use. Based on the values for height and weight, body mass index (BMI, weight/height^2; kg/m^2) was computed. BMI was categorized into 4 groups: <25, 25–29.9, 30.0–34.9 and ≥35.0 kg/m^2. Underweight (<18.5 kg/m^2) and normal weight (18.5–24.9 kg/m^2) were combined and used as the reference category, as less than 1% of the cohort were in the underweight category. TSC level was categorized into quintiles based on the distribution observed in our male cohort population. The first (lowest) quintile was used as the reference category. Participants were asked if they smoke cigarettes now, the answer choices were yes, regularly; yes, occasionally; no. Similarly, they were asked if they ever smoked cigarettes. The number of cigarettes usually smoked per day and the age at starting and quitting smoking were recorded. We classified smoking status into categories never, former and current: ≤10 cig/day, 11–19 cig/day and ≥20 cig/day, respectively. Individuals who had never smoked cigarettes regularly or occasionally were considered never smokers, and those who reported previous or present regular or occasional smoking were classified as former or current smokers. For alcohol consumption, we grouped participants into four groups according to reported frequency of alcohol consumption (never or former, a few times per year, 1–4 times per month, 2–7 times per week). Furthermore, individuals were classified into five groups according to their total amount of ethanol consumed from all beverages (beer, wine, vodka): non-drinkers, 0.1–9.9 g/week, 10.0–24.9 g/week, 25.0–99.9 g/week, and ≥100 g/week. The cut-points were selected on the basis of cohort distribution and aiming to retain extreme categories and sufficient number of cases in sub-groups. Occasional drinkers (a few times per year) or participants with very light alcohol consumption (0.1–9.9 g ethanol/week) were used as a reference, because we assumed that they would have the lowest risk of cancer. The non-drinkers' risk may be increased, as they might include some of the former heavy drinkers that had stopped drinking at the time of the interview due to ill health possibly related to cancer. Blood pressure was categorized into groups based on the recommended classification by the European Society of Hypertension (23).

Statistical Analysis

The strength of association between risk factors and kidney cancer incidence was examined using the age-adjusted and multivariable-adjusted incidence hazard ratios (HR) and corresponding 95% confidence intervals (CI). Multivariate Cox proportional hazards models, stratified by study to control for differences in study-specific effects, were used to calculate HR. Confounders were selected a priori and included age (<50, 50–54, ≥55), education level (primary, unfinished secondary, secondary and high school), BMI (<25.0 kg/m^2, 25.0–29.9 kg/m^2, 30.0–34.9 kg/m^2, ≥35.0 kg/m^2) and cigarette smoking (never, former, ≤10 cig/day, 11–19 cig/day, ≥20 cig/day). Alcohol consumption and TSC level were also considered; however, adjustment for them had minimal effects on the results, so these variables were ignored in the final analysis. To examine whether BMI possibly modify the association of blood pressure with risk of kidney cancer among men, we estimated HRs in strata of BMI, i.e. in men with normal weight (BMI <25) and in overweight (BMI ≥25). Tests for linear dose-response trends were performed by fitting ordinal exposure variables as continuous terms in the proportional hazards model or by estimating HRs, associated with an increase in 1 unit of BMI or TSC and 10 units of blood pressure. We tested for linear trend for smoking and alcohol after excluding never or former smokers and never or former drinkers, respectively. We carried out sensitivity analyses excluding 40 participants who reported use of lipid-lowering medication or 487 participants who reported ever

use of antihypertensive medication to examine the risk of TSC or hypertension, respectively, and results were similar to those reported here. Proportional hazards assumption was checked by including interaction term of time and each covariate. The interaction term was non-significant at the 5% level in any of the models.

All statistical analyses were performed using the Statistical Package SPSS 19. All p-values were based on two-sided tests and, if less than 0.05, considered statistically significant.

RESULTS

Baseline characteristics of participants are described in Table 1. Among the 6,849 men with mean follow-up time of 19.2 ± 8.6 years, 79 incident cases of kidney cancer were diagnosed. About 73% of participants were overweight (BMI ≥ 25) and 22% obese (BMI ≥ 30). The proportion of men with hypertension (systolic blood pressure ≥ 140 mmHg and/or diastolic blood pressure ≥ 90 mmHg) was 50%. About 7% of participants reported ever use of antihypertensive medication. Among men with Grade 3 hypertension (systolic and diastolic blood pressure ≥ 180 and/or ≥ 110 mmHg, respectively) 39% ever used antihypertensive medication (data not shown).

Table 2 shows the HRs of kidney cancer in relation to BMI, number of cigarettes smoked per day, pack-years of smoking, frequency and amount of alcohol consumption, and TSC level. Men with BMI ≥ 35 had a substantially higher risk of kidney cancer than those with BMI < 25.0 (HR 3.00, 95% CI 1.10–8.19, P_{trend} = 0.07). The risks were not statistically significantly increased in other BMI groups. When modelling BMI as a continuous variable, we found a 7% increase in risk of kidney cancer per 1 unit of BMI. There was no evidence of an association between smoking, alcohol consumption or TSC level and risk of kidney cancer (Table 2).

Among men with the elevated blood pressure, we observed a relative risk of 1.07 (95 % CI 0.94–1.21) and 1.18 (95 % CI 0.97–1.45), for each additional 10 mmHg of systolic or diastolic blood pressure, respectively (data not shown). The analysis showed an increase in risk of kidney cancer associated with blood pressure among overweight men (BMI ≥ 25) (Table 3). The HR of kidney cancer was 1.10 (95% CI 0.96–1.25) per 10 mmHg of systolic blood pressure and 1.26 (95% CI 1.01–1.56) per 10 mmHg of diastolic blood pressure. Furthermore, the HR for developing kidney cancer among men in the highest (Grade III) hypertension category (≥ 180 mmHg systolic and/or ≥ 110 mmHg diastolic blood pressure) compared to < 120 mmHg and < 80 mmHg, respectively, was 10.61 (95% CI 1.22–92.43). This positive association was not seen among men with BMI <25 kg/m^2.

Table 1. *Selected baseline characteristics of study participants, 1978–2008 (N = 6,849)*

Characteristic	Statistic Mean ± SD or n (%)
No. of participants	6,849
Age at entry, years	52.6 ± 5.7
Age at kidney cancer diagnosis, years	67.9 ± 7.1
Height, cm^2	172.3 ± 6.4
BMI, kg/m^2	27.4 ± 3.8
BMI ≥ 25	5,011 (73.2)
BMI ≥ 30	1,477 (21.6)
Total serum cholesterol, mmol/l	6.0 ± 1.1
Current smokers	3,082 (45.0)
Alcohol consumption	
Never or former	559 (8.2)
2–7 times per week	376 (5.5)
Hypertension	
Grade ≥ 1 hypertension[a]	3,430 (50.1)
Grade 3 hypertension[b]	396 (5.8)
Antihypertensive medication, ever: yes	487 (7.1)
Statins, ever: yes	41 (0.6)
Education: primary	1,568 (22.9)
Follow-up, years	19.2 ± 8.6
Person-years	131,322.1

SD – standard deviation; BMI – body mass index
[a]systolic blood pressure ≥ 140 and/or diastolic blood pressure ≥ 90 mmHg; [b]systolic blood pressure ≥ 180 and/or diastolic blood pressure ≥ 110 mmHg

DISCUSSION

The present study supports existing evidence that BMI is associated with an increased risk of kidney cancer in a dose-response manner. In addition, we observed a positive relation between blood pressure and risk of kidney cancer in overweight men. These results are consistent with previous epidemiological studies and reviews (9, 10, 12, 14–17, 24–26), and provide additional information on the link between BMI, hypertension and kidney cancer.

A number of studies have assessed the relation of hypertension to kidney cancer risk within categories of BMI (16, 24, 26). An increased risk of kidney cancer associated with elevated blood pressure independently of BMI was found (16, 24). Our data show that among overweight, increased blood pressure was associated with an increase in kidney cancer. There was no association among men with normal weight, however, small number of men with elevated blood pressure and normal BMI limited the analysis. In our study, only 7% of individuals reported ever using antihypertensive medication, although approximately half of the participants had hypertension. Furthermore, only 39% ever used antihypertensive medication among men with Grade 3 hypertension. Our findings potentially suggest that untreated and thus poorly controlled blood pressure may be related to an increased cancer risk, in agreement with previous studies (3, 14, 24).

Cigarette smoking has been found to be a weak to moderate risk factor for kidney cancer (5, 6). In the present study, we found no significantly increased risk. In agreement with report from several studies (7, 8, 26), our findings provide evidence that alcohol consumption is not associated with the increased risk of developing kidney cancer. TSC level was not related to increased kidney cancer risk in our study, similar to other analyses (19, 20).

The mechanisms that have been hypothesized to influence kidney cancer development in obese individuals include low-

Table 2. *Hazard ratios of kidney cancer by cigarette smoking, alcohol consumption, height and total serum cholesterol levels, 1978–2008 (N = 6,849)*

Variable	No. of cases/No. of subjects	Age adjusted HR (95% CI)	Multivariable-adjusted HR (95% CI)
BMI (kg/m^2)[a]			
< 25.0	17/1,838	1	1
25.0–29.9	41/3,534	1.12 (0.63–1.97)	1.16 (0.65–2.06)
30.0–34.9	16/1,264	1.33 (0.67–2.64)	1.40 (0.70–2.80)
≥ 35.0	5/213	3.01 (1.11–8.17)	3.00 (1.10–8.19)
BMI, continuous (per 1 kg/m^2)		1.07 (1.01–1.13)	1.07 (1.01–1.14)
Smoking status (no. of cigarettes per day)[b]			
Never	25/2,090	1 (reference)	1 (reference)
Former	21/1,677	1.18 (0.66–2.11)	1.13 (0.63–2.03)
≤ 10	11/964	1.17 (0.58–2.38)	1.18 (0.58–2.41)
11–19	3/588	0.56 (0.17–1.86)	0.57 (0.17–1.91)
≥ 20	19/1,530	1.55 (0.85–2.82)	1.57 (0.85–2.89)
P_{trend}		0.36	0.29
Cumulative amount of smoking (pack-years)[b]			
Never	25/2,090	1 (reference)	1 (reference)
Former	21/1,677	1.18 (0.66–2.11)	1.13 (0.63–2.03)
< 10	4/433	0.89 (0.31–2.55)	0.85 (0.30–2.46)
10–19	12/817	1.46 (0.73–2.75)	1.51 (0.75–3.04)
20–29	10/806	1.32 (0.63–2.75)	1.38 (0.65–2.90)
≥ 30	7/1,026	1.04 (0.44–2.46)	1.10 (0.46–2.62)
P_{trend}		0.67	0.29
Alcohol consumption (frequency)[c]			
Never or former	6/559	1.19 (0.45–3.17)	1.16 (0.44–3.12)
A few times per year	12/1,195	1 (reference)	1 (reference)
1–4 times per month	59/4,719	1.39 (0.74–2.59)	1.31 (0.70–2.47)
2–7 times per week	2/376	0.70 (0.16–3.15)	0.64 (0.14–2.89)
P_{trend}		0.47	0.82
Ethanol intake (g/week)[c]			
Non-drinkers	6/559	1.25 (0.47–3.32)	1.21 (0.46–3.24)
0.1–9.9	12/1,281	1 (reference)	1 (reference)
10.0–24.9	31/2,374	1.50 (0.77–2.92)	1.42 (0.72–2.79)
25.0–99.9	22/1,772	1.46 (0.72–2.95)	1.35 (0.66–2.77)
≥ 100.0	8/863	1.15 (0.47–2.82)	1.04 (0.41–2.61)
P_{trend}		0.49	0.66
TSC (mmol/l)[d]			
< 5.02	17/1,362	1 (reference)	1 (reference)
5.02–5.62	9/1,364	0.52 (0.23–1.16)	0.51 (0.23–1.14)
5.63–6.15	13/1,361	0.76 (0.37–1.56)	0.73 (0.35–1.50)
6.16–6.85	23/1,391	1.36 (0.72–2.54)	1.25 (0.66–2.35)
≥ 6.86	17/1,371	1.06 (0.54–2.07)	1.00 (0.51–1.98)
TSC, continuous, per 1 mmol/l		1.04 (0.85–1.27)	1.02 (0.83–1.25)

[a]In multivariable analysis, adjusted for age, smoking status, education.
[b]In multivariable analysis, adjusted for age, education, BMI. Test for trend was carried out after exclusion of never and former smokers.
[c]In multivariable analysis, adjusted for age, smoking status, education, BMI. Test for trend was carried out after exclusion of never and former drinkers.
[d]In multivariable analysis, adjusted for age, smoking status, education, BMI.
TSC –- total serum cholesterol

Table 3. *Hazard ratios of kidney cancer according to systolic and diastolic blood pressure by BMI, 1978–2008 (N = 6,849)*

Variable	BMI					
	< 25 kg/m^2			≥ 25 kg/m^2		
	No. of cases/No. of subjects	Age adjusted HR (95% CI)	Multivariable-adjusted HR (95% CI)[a]	No. of cases/No. of subjects	Age adjusted HR (95% CI)	Multivariable-adjusted HR (95% CI)[b]
Systolic blood pressure (mmHg)						
< 120	7/527	1 (reference)	1 (reference)	5/720	1 (reference)	1 (reference)
120–129	5/465	1.81 (0.26–2.55)	0.80 (0.25–2.55)	13/1026	2.01 (0.72–5.64)	1.92 (0.68–5.40)
130–139	2/347	0.46 (0.10–2.23)	0.50 (0.10–2.41)	15/1073	2.33 (0.85–6.43)	2.20 (0.79–6.10)
140–159	2/376	0.50 (0.10–2.45)	0.57 (0.12–2.81)	23/1487	2.90 (1.10–7.66)	2.66 (0.99–7.10)
160–179	1/97	1.28 (0.16–10.55)	1.33 (0.16–11.10)	3/507	1.44 (0.34–6.08)	1.27 (0.30–5.43)
≥ 180	0/26	–	–	3/198	4.48 (1.05–19.14)	3.90 (0.90–16.96)
Systolic blood pressure, continuous (per 10 mmHg)		0.93 (0.68–1.27)	0.96 (0.70–1.31)		1.12 (0.98–1.27)	1.10 (0.96–1.25)
Diastolic blood pressure (mmHg)						
< 80	8/776	1 (reference)	1 (reference)	8 / 1031	1 (reference)	1 (reference)
80–84	2/360	0.57 (0.12–2.69)	0.62 (0.13–2.94)	9 / 843	1.46 (0.56–3.79)	1.38 (0.53–3.59)
85–89	6/257	2.53 (0.88–7.32)	2.87 (0.98–8.43)	12 / 818	2.06 (0.84–5.04)	1.98 (0.81–4.87)
90–99	1/340	0.35 (0.04–2.83)	0.35 (0.04–2.84)	20 / 1439	2.01 (0.88–4.56)	1.87 (0.82–4.29)
100–109	0/79	–	–	9 / 607	2.47 (0.95–6.42)	2.32 (0.88–6.12)
≥ 110	0/26	–	–	4 / 273	3.33 (1.00–11.13)	2.95 (0.86–10.04)
Diastolic blood pressure, continuous (per 10 mmHg)		0.92 (0.56–1.51)	0.95 (0.58–1.55)		1.28 (1.04–1.58)	1.26 (1.01–1.56)
Systolic and diastolic blood pressure (mmHg)						
< 120 and < 80	5/432	1 (reference)	1 (reference)	1 / 469	1 (reference)	1 (reference)
120–129 and/or 80–84	3/419	0.63 (0.15–2.62)	0.63 (0.15–2.63)	12 / 792	7.79 (1.01–59.90)	7.12 (0.92–54.82)
130–139 and/or 85–89	6/343	1.59 (0.48–5.24)	1.85 (0.55–6.18)	10 / 964	5.50 (0.70–43.00)	5.18 (0.66–40.62)
140–159 and/or 90–99	2/476	0.44 (0.09–2.31)	0.48 (0.09–2.52)	26 / 1678	8.89 (1.21–55.55)	8.05 (1.09–59.64)
160–179 and/or 100–109	1/127	1.09 (0.13–9.41)	1.24 (0.14–10.87)	8 / 753	7.16 (0.89–57.38)	6.36 (0.79–51.48)
≥ 180 and/or ≥ 110	0/41	–	–	5 / 355	12.65 (1.47–108.81)	10.67 (1.22–93.23)
P_{trend}		0.73	0.77		0.03	0.06

[a]Adjusted for age, smoking status, education
[b]Adjusted for age, smoking status, education, BMI

grade chronic inflammatory state, lipid peroxidation and oxidative stress. In addition, excess body fat affects circulating insulin levels and it increases the risk of high blood pressure – factors positively related to the development of kidney cancer (3, 9). The biologic mechanisms underlying the association between hypertension and kidney cancer are unclear but are hypothesized to include chronic renal hypoxia and lipid peroxidation with formation of reactive oxygen species (3).

The main strength of this study was the prospective design, with data collected up to 30 years prior to the cancer diagnosis, thus minimizing the risk of recall bias and bias due to reverse causation. The available data allowed us to test for a number of potential confounding factors. Since most of these factors are measured with a certain degree of error, residual confounding cannot be completely ruled out. The use of data at baseline was a weakness of the study, because during the long follow-up the BMI of study participants, levels of blood pressure, TSC or other factors may have changed; thus, it is likely that misclassification might have occurred. There is a potential for misclassification of disease due to relatively low rate of pathological confirmation of kidney cancer; this may have attenuated the effect estimates toward null. No information on morphological verification of kidney cancer was available for this study, however, it was 72.4% in Lithuania during the period 1998–2002 and 76.7% during the period 2003–2007 (27, 28). The present study was also limited by the choice of covariates, since information on potential confounding factors (e.g., dietary characteristics, occupation, other renal diseases, family history of cancer) is lacking. Further limitations include the lack of statistical power due to the small sample size, thus we cannot entirely rule out the possibility of chance findings. The modest sample size also limited our ability to perform a more detailed analysis of the data, e.g. by antihypertensive medication use or an interaction analysis.

A survey in the WHO MONICA study showed that in Eastern European countries in the 1980s and the early 1990s the mean BMI was much higher than in Western Europe (29). The mean BMI of the Kaunas population (representing Lithuania) was the highest among 34 populations from different countries (29). Furthermore, the prevalence of overweight men has been increasing during the subsequent decades in Lithuania (30). Hypertension is a major chronic disease, estimated to affect about 70% of the Lithuanian men with increasing prevalence that is higher than in most other populations (30). The high prevalence of overweight and hypertension among men in Lithuania and other Eastern European countries is likely to have contributed to the high incidence rates of kidney cancer. Overweight and hypertension are preventable exposures; therefore, their control could substantially reduce the incidence of kidney cancer.

CONCLUSION

In conclusion, results suggest the importance of increased BMI in the development of kidney cancer among men in Lithuania. Hypertension appears to be associated with risk of kidney cancer in overweight men, although the assessment was limited by the lack of statistical power. Our findings imply that effective control of weight and hypertension may be important in the prevention of this type of cancer.

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Conflict of Interests

None declared

REFERENCES

1. Ferlay J, Ervik M, Lam F, Colombet M, Mery L, Piñeros M, et al. Global cancer observatory: cancer today [Internet]. Lyon: International Agency for Research on Cancer; 2018 [cited 2019 Oct 31]. Available from: https://gco.iarc.fr/today/home.
2. Li P, Znaor A, Holcatova I, Fabianova E, Mates D, Wozniak MB, et al. Regional geographic variations in kidney cancer incidence rates in European countries. Eur Urol. 2015;67(6):1134-41.
3. Chow WH, Dong LM, Devesa SS. Epidemiology and risk factors for kidney cancer. Nat Rev Urol. 2010;7(5):245-57.
4. Znaor A, Lortet-Tieulent J, Laversanne M, Jemal A, Bray F. International variations and trends in renal cell carcinoma incidence and mortality. Eur Urol. 2015;67(3):519-30.
5. Personal habits and indoor combustions. IARC Monogr Eval Carcinog Risks Hum. 2012;100(Pt E):1-538.
6. Weikert S, Ljungberg B. Contemporary epidemiology of renal cell carcinoma: perspectives of primary prevention. World J Urol. 2010;28(3):247-52.
7. Song DY, Song S, Song Y, Lee JE. Alcohol intake and renal cell cancer risk: a meta-analysis. Br J Cancer. 2012;106(11):1881-90.
8. Wozniak MB, Brennan P, Brenner DR, Overvad K, Olsen A, Tjønneland A, et al. Alcohol consumption and the risk of renal cancers in the European prospective investigation into cancer and nutrition (EPIC). Int J Cancer. 2015;137(8):1953-66.
9. World Cancer Research Fund International; American Institute for Cancer Research. Diet, nutrition, physical activity and kidney cancer, revised 2018 [Internet]. World Cancer Research Fund International; 2018 [cited 2019 Oct 31]. Available from: https://www.wcrf.org/sites/default/files/Kidney-cancer-report.pdf.
10. Häggström C, Rapp K, Stocks T, Manjer J, Bjørge T, Ulmer H, et al. Metabolic factors associated with risk of renal cell carcinoma. PLoS One. 2013;8(2):e57475. doi:10.1371/journal.pone.0057475.
11. Stocks T, Bjørge T, Ulmer H, Manjer J, Häggström C, Nagel G, et al. Metabolic risk score and cancer risk: pooled analysis of seven cohorts. Int J Epidemiol. 2015;44(4):1353-63.
12. Shen T, Shu XO, Xiang YB, Li HL, Cai H, Gao YT, et al. Association of hypertension and obesity with renal cell carcinoma risk: a report from the Shanghai Men's and Women's Health Studies. Cancer Causes Control. 2015;26(8):1173-80.
13. Keum N, Greenwood DC, Lee DH, Kim R, Aune D, Ju W, et al. Adult weight gain and adiposity-related cancers: a dose-response meta-analysis of prospective observational studies. J Natl Cancer Inst. 2015 Mar 10;107(2). pii: djv088.
14. Chow WH, Gridley G, Fraumeni JF Jr, Järvholm B. Obesity, hypertension, and the risk of kidney cancer in men. N Engl J Med. 2000;343(18):1305-11.
15. Pischon T, Lahmann PH, Boeing H, Tjønneland A, Halkjaer J, Overvad K, et al. Body size and risk of renal cell carcinoma in the European Prospective Investigation into Cancer and Nutrition (EPIC). Int J Cancer. 2006;118(3):728-38.
16. Sanfilippo KM, McTigue KM, Fidler CJ, Neaton JD, Chang Y, Fried LF, et al. Hypertension and obesity and the risk of kidney cancer in two large cohorts of US men and women. Hypertension. 2014;63(5):934-41.
17. Golabek T, Bukowczan J, Szopinski T, Chlosta P, Lipczynski W, Dobruch J, et al. Obesity and renal cancer incidence and mortality - a systematic review of prospective cohort studies. Ann Agric Environ Med. 2016;23(1):37-43.

18. Van Hemelrijck M, Garmo H, Hammar N, Jungner I, Walldius G, Lambe M, et al. The interplay between lipid profiles, glucose, BMI and risk of kidney cancer in the Swedish AMORIS study. Int J Cancer. 2012;130(9):2118-28.
19. Strohmaier S, Edlinger M, Manjer J, Stocks T, Bjørge T, Borena W, et al. Total serum cholesterol and cancer incidence in the Metabolic Syndrome and Cancer Project (Me-Can). PLoS One. 2013;8(1):e54242. doi:10.1371/journal.pone.0054242.
20. Zhang C, Yu L, Xu T, Hao Y, Zhang X, Liu Z, et al. Association of dyslipidemia with renal cell carcinoma: a 1:2 matched case-control study. PLoS One. 2013;8(3):e59796. doi:10.1371/journal.pone.0059796.
21. Everatt R, Tamosiunas A, Kuzmickiene I, Virviciute D, Radisauskas R, Reklaitiene R, et al. Alcohol consumption and risk of gastric cancer: a cohort study of men in Kaunas, Lithuania, with up to 30 years follow-up. BMC Cancer. 2012 Oct 15;12:475. doi:10.1186/1471-2407-12-475.
22. Siedel J, Hagele EO, Ziegenhorn J, Wahlefeld AW. Reagent for the enzymatic determination of serum total cholesterol with improved lipolytic efficiency. Clin Chem. 1983;29(6):1075-80.
23. ESH/ESC Task Force for the Management of Arterial Hypertension. 2013 Practice guidelines for the management of arterial hypertension of the European Society of Hypertension (ESH) and the European Society of Cardiology (ESC). J Hypertens. 2013 Oct;31(10):1925-38.
24. Weikert S, Boeing H, Pischon T, Weikert C, Olsen A, Tjonneland A, et al. Blood pressure and risk of renal cell carcinoma in the European Prospective Investigation into Cancer and Nutrition. Am J Epidemiol. 2008;167(4):438-46.
25. Wang F, Xu Y. Body mass index and risk of renal cell cancer: A dose-response meta-analysis of published cohort studies. Int J Cancer. 2014;135(7):1673-86.
26. Macleod LC, Hotaling JM, Wright JL, Davenport MT, Gore JL, Harper J, et al. Risk factors for renal cell carcinoma in the VITAL Study. J Urol. 2013;190(5):1657-61.
27. Curado MP, Edwards B, Shin HR, Storm H, Ferlay J, Heanue M, et al. Cancer incidence in five continents, volume IX. IARC Sci Publ. 2007;(160):1-896.
28. Forman D, Bray F, Brewster DH, Gombe Mbalawa C, Kohler B, Piñeros M, et al. Cancer incidence in five continents, volume X. IARC Sci Publ. 2014;(164):1-1365.
29. Silventoinen K, Sans S, Tolonen H, Monterde D, Kuulasmaa K, Kesteloot H, et al.; WHO MONICA Project. Trends in obesity and energy supply in the WHO MONICA Project. Int J Obes Relat Metab Disord. 2004 May;28(5):710-8.
30. Tamosiunas A, Klumbiene J, Petkeviciene J, Radisauskas R, Vikhireva O, Luksiene D, et al. Trends in major risk factors and mortality from main non-communicable diseases in Lithuania, 1985-2013. BMC Public Health. 2016 Aug 4;16:717. doi: 10.1186/s12889-016-3387-0.

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