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Original Article

Ambient particulate matter exposure and urologic cancer: a longitudinal nationwide cohort study

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Abstract: Increased particulate matter (PM) exposure is positively associated with increased incidence and mortality of many human malignancies. However, evidence of urologic cancer is limited. We aimed to evaluate the association between PM_{10} exposure and the relative risk of urologic cancer. This nationwide longitudinal cohort study included 231,997 participants who underwent a baseline health examination in 2008 from the National Health Information Database of Korea. The primary endpoint was newly diagnosed urologic cancer according to PM_{10} exposure. Of the total 231,99 participants, 50,677 developed urologic cancer during a median follow-up of 6.7 years. After controlling for confounding factors, participants in the high PM_{10} exposure group had a higher risk of kidney cancer (hazard ratio [HR] 1.111, 95% confidence interval [CI] 1.068-1.157) and prostate cancer (HR 1.083, 95% CI 1.058-1.109) than those in the low PM_{10} exposure group. However, in urothelial cell carcinoma, there was no significant increase in the HRs in the high PM_{10} exposure group. For kidney cancer, participants with the following characteristics were more susceptible: age < 65 years, female sex, decreased regular physical activity, current smoking, no diabetes, no hypertension, normal body mass index, and desirable total cholesterol level. For prostate cancer, participants with the following characteristics were more susceptible: decreased regular physical activity, current smoking, and no hypertension. High PM_{10} exposure is associated with an increased risk of overall urologic cancers, especially kidney and prostate cancer.

Keywords: Urologic cancer, particulate matter exposure, kidney cancer, prostate cancer, urothelial cell carcinoma

Introduction

Air pollution has been associated with detrimental effects on human health including increased risk of premature mortality, cardiovascular and respiratory diseases, adverse birth outcomes, and several cancers [1, 2]. The World Health Organization has reported that ambient air pollution and household air pollution are associated with 7 million premature deaths annually, and has declared air pollution as the "silent killer" [3]. Air pollution is a complex mixture of pollutants including sulfur oxides, nitrogen oxides, ambient ozone, and particulate matter (PM). PM, a mixture of toxic and carcinogenic substances, is classified by the aerodynamic diameter of particles: PM_{10} is < 10 μm in diameter; $PM_{2.5}$ is < 2.5 μm; $PM_{0.1}$ particles are < 0.1 μm. PM can easily penetrate the respiratory system and enter the blood, causing extensive inflammatory reactions, endothelial cell damage, increased oxidative stress, and ultimately carcinogenesis [4-6].

Ambient PM has been designated as a Group 1 human carcinogen by the International Agency for Research on Cancer (IARC) in 2013 [7]. In a meta-analysis originated by the IARC, the relative risk for lung cancer associated with $PM_{2.5}$ and PM_{10} was 1.09 (95% confidential interval [CI]: 1.04, 1.14), and 1.08 (95% CI: 1.00, 1.17), respectively [8]. In addition, a growing body of evidence has demonstrated that increased PM exposure is positively associated with the increased incidence and mortality of many human malignancies including breast cancer [9, 10], colorectal cancer [11], thyroid cancer [12], liver cancer [13], and childhood cancer

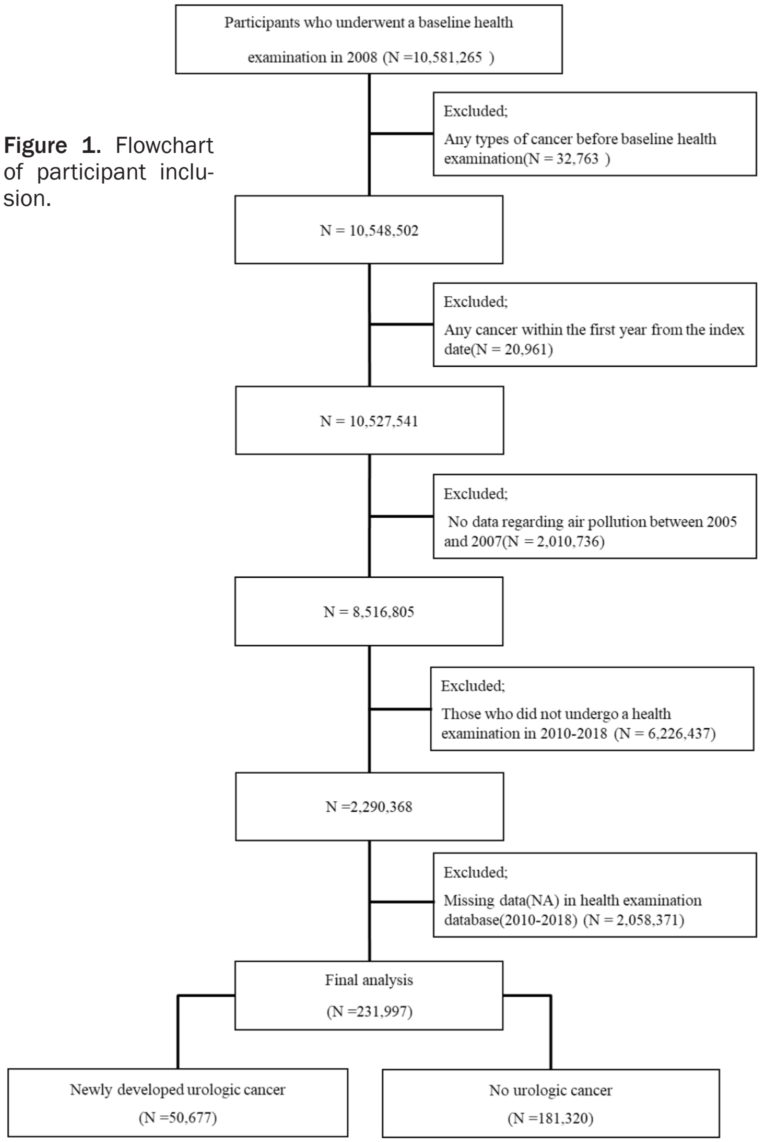

Figure 1. Flowchart of participant inclusion.

[14]. Although there is sufficient evidence regarding the association between PM exposure and human malignancies, evidence for urologic cancer is limited [15]. Thus, in this nationwide longitudinal cohort study, we aimed to evaluate the association between PM_{10} exposure and the relative risks of urologic cancers such as kidney cancer, prostate cancer, and urothelial cell carcinoma.

Methods

Data source

We used a customized database (DB) from the National Health Information (NHI) DB of the National Health Insurance Service (NHIS), which covers nearly the entire South Korean population. The NHIS maintains a health examination database for all insured persons in South Korea consisting of anthropometric measurements, laboratory tests, and self-report questionnaires. The NHI DB includes qualification information, insurance rates, health check-up results, treatment details, long-term care insurance data for the elderly, treatment status, cancer, and rare disease registration information. The NHIS has provided data including a sample cohort DB, customized DB, health disease index for academic research in the health and medical sector.

Study population

This study received exemption status from the Institutional Review Board at Seoul St. Mary's Hospital and Dankook University. Participants who underwent a baseline health examination in 2008 were included in the NHI DB (N= 10,581,265). We excluded participants with any cancer within the first year from the index data (N=20,961), those with no data regarding air pollution between 2005 and 2007 (N=2,010,736), those who did not receive more than four consecutive health examinations from 2010 to 2018 (N=6,226,437), and those with missing data on health examination (N=2,058,371). A total of 231,997 participants were included in the final analysis (**Figure 1**). The primary endpoint was newly diagnosed urologic cancer (N=50,677). **Figure 2** is a diagram to help understand the participant timeline.

Definition of urologic cancer

We focused on newly diagnosed urologic cancers, such as kidney cancer, prostate cancer, and urothelial cell carcinoma. Kidney cancer was defined as C64x according to ICD-10

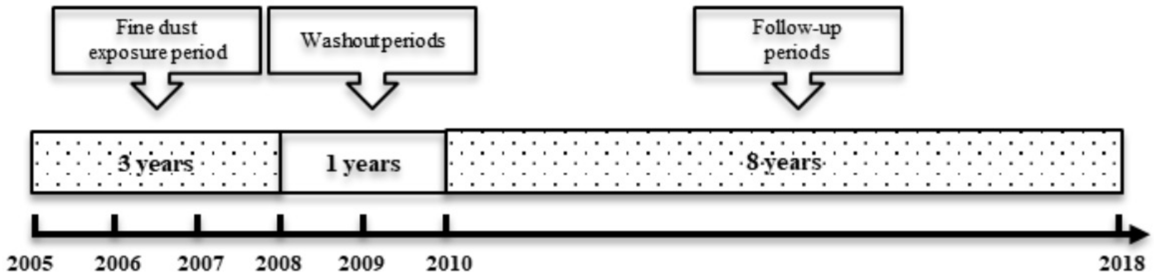

Figure 2. Diagram for a timeline of participants.

codes. Prostate cancer was defined as C61 and urothelial cell carcinoma was defined as C65x, C66x, and C67 according to ICD-10 codes. Among the newly diagnosed urologic cancer cases (N=50,677), 9,736 were kidney cancer (19.2%), 28,440 were prostate cancers (56.1%), and 12,501 were urothelial cell carcinoma (24.6%).

Estimation of individual particulate matter exposure

We used air pollution data from AirKorea provided by the Korean Environment Corporation which collects local pollution information through the National Ambient Air Quality Monitoring Information System and provides it through the AirKorea website [16]. In South Korea, PM_{10} standard was newly established and has been applied since 1995. In 2008, 426 measuring stations were installed nationwide (as of the end of December 2008) [17].

Covariate assessment

Regular physical activity was divided into three groups: no exercise, 1-4 times per week, and ≥ 5 days per week. Alcohol consumption was divided into three groups: non-drinkers, drinkers (2-8 times per month), and heavy drinkers (≥ 4 times per week). There were three groups of smokers: non-smokers, ex-smokers, and smokers. Diabetes mellitus (DM) and hypertension were classified according to the presence or absence of disease using the ICD-10 codes. There were three groups of body mass index (BMI): below 25 (underweight and normal), 25-29.9 (overweight), and over 30 kg/m^2 (obesity) [18]. There were three groups of fasting blood glucose levels: normal, pre-diabetic, and diabetic [19]. There were four groups of total cholesterol: desirable level (< 200 mg/dL), borderline high level (200-239 mg/dL), and high level (≥ 240 mg/dL) [20].

Statistical analysis

Statistical analyses were performed using R version 4.0.3 (2020-10-10) and SPSS Statistics version 25.0 (SPSS Inc.). R was used for data preprocessing and visualization of the PM_{10} data distribution. The baseline demographic data of the participants were compared using the independent t-test for continuous variables and the chi-squared test for categorical variables. The incidence rates of urologic cancer were calculated per 1,000 person-years. The association between the incidence of urologic cancer and PM_{10} exposure was assessed using multivariate Cox proportional hazards regression analysis. All statistical tests were two-tailed, and the significance level was set at *P*-values < 0.05.

Results

Baseline statistics of air pollutant

We used 3-year average PM_{10} concentration data measured at 398 stations from 2005 to 2007 (based on 2008). To categorize the participants according to PM_{10} concentration, we explored the PM_{10} concentration data. The mean and median PM_{10} concentration were 56.24 and 56 μg/m^3, respectively. The skewness and kurtosis were 0.133 and 0.139, respectively (**Figure 3**). There are four criteria for PM_{10} concentrations in South Korea: good (0-30 μg/m^3), moderate (31-80 μg/m^3), unhealthy (81-150 μg/m^3), and very unhealthy (> 150 μg/m^3) [21]. Due to the nature of the data, it was not possible to classify the participants according to the Korean criteria for PM_{10} concentration. Considering the characteristics of the data regarding PM_{10} concentration, the participants were divided into two groups according to the median concentration of PM_{10} (56 μg/m^3). The location-specific distribution of urologic cancer incidence and PM_{10} concentra-

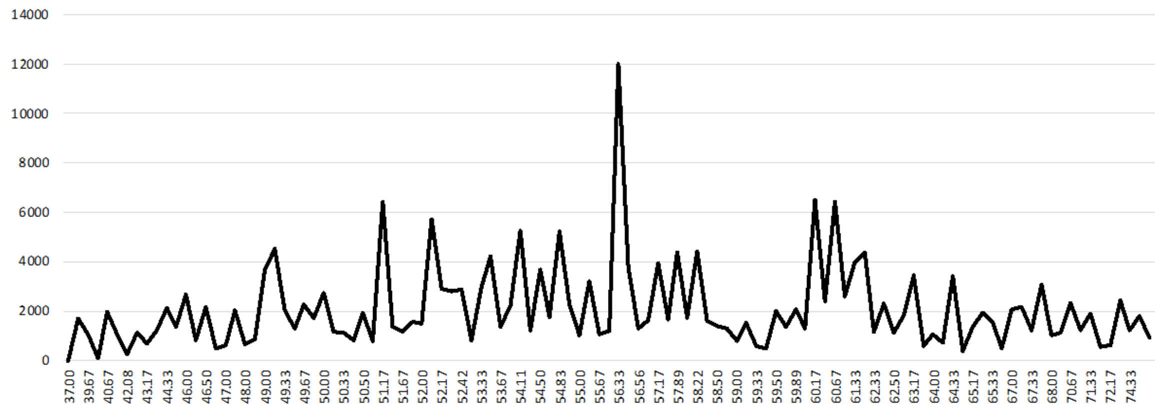

Figure 3. Distribution of PM_{10} concentration. X-axis: PM_{10} concentration (μg/m³), Y-axis: frequency.

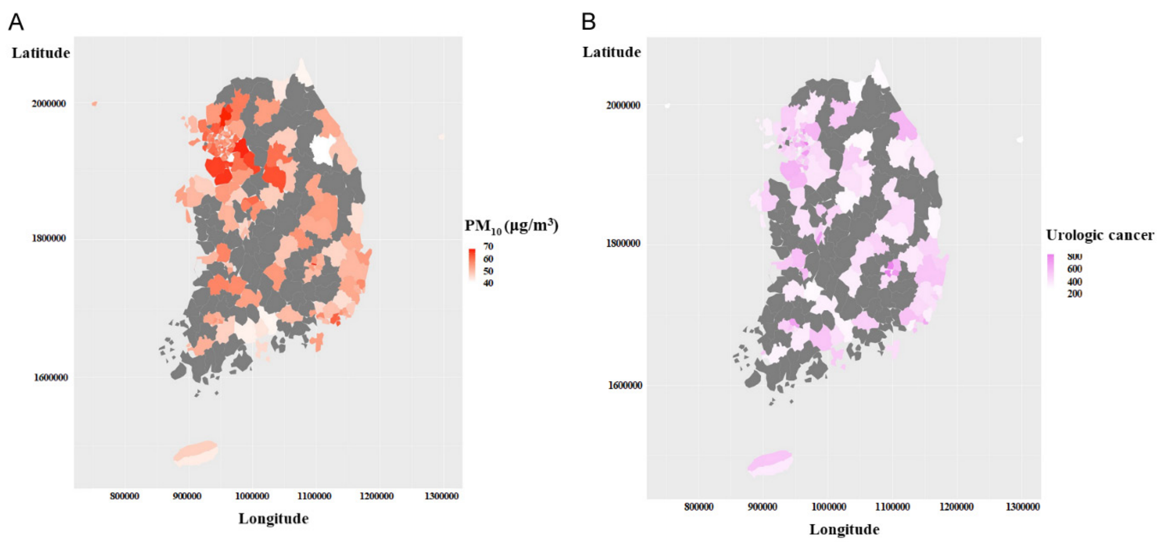

Figure 4. Distribution of (A) PM_{10} concentration and (B) incidence of urologic cancer in South Korea.

tion in South Korea showed similar patterns as shown in **Figure 4**.

Baseline characteristics of the participants

Of the total 231,99 participants, 21.8% developed urologic cancer during the median follow-up of 6.7 years (**Table 1**). Of the total 50,677 urologic cancer patients, 56.1% had prostate cancer, 24.7% had urothelial cell carcinoma, and 19.2% had kidney cancer. The age ratio of those aged ≥ 65 years was 49.5%, similar to that of those aged < 60 years. The proportion of female was 77.3%. Fifty percent of participants did not exercise regularly, 56.8% of the total did not drink alcohol. 60.7% of the total were non-smokers. Only 28.5% had hypertension and 12.4% had DM.

We divided the extracted data into two groups based on PM_{10} concentration (**Table 2**). According to the PM_{10} concentration, there were significant differences in almost all baseline characteristics. Regardless of the occurrence of urological cancer, the proportion of participants older than 65 years and males was significantly higher in the high PM_{10} group. The prevalence of comorbidities such as DM and hypertension was also higher in the high PM_{10} group.

Risk of urologic cancer according to the PM_{10} exposure

Table 3 presents the HRs (95% CIs) for urologic cancer according to PM_{10} concentrations. High PM_{10} exposure was associated with an increased overall risk of urologic cancer. It was

Table 1. Demographics characteristics

Variables		N	%
Class	No urologic cancer	181,320	78.2
	Newly developed urologic cancer	50,677	21.8
PM_{10} exposure	Low PM_{10} group (Under 56 μg/m^3)	123,081	53.1
	High PM_{10} group (Over 56 μg/m^3)	108,916	46.9
Age	< 65 years	117,210	50.5
	≥ 65 years	114,787	49.5
Gender	Male	179,255	77.3
	Female	52,742	22.7
Regular physical activity	No exercise	116,041	50.0
	1-4 times per week	82,687	35.6
	5 or more times per week	33,269	14.3
Alcohol consumption	No Alcohol	131,840	56.8
	2-8 times per month	66,146	28.5
	4 or more times per week	34,011	14.7
Smoking	Non-smoker	140,864	60.7
	Ex-smoker	30,289	13.1
	Smoker	60,844	26.2
Hypertension	No	165,945	71.5
	Yes	66,052	28.5
Diabetes mellitus	No	203,175	87.6
	Yes	28,822	12.4
Death	No	193,334	83.3
	Yes	38,663	16.7
BMI (kg/m^2)	Less than 25	154,449	66.6
	25-29.9	70,804	30.5
	Over 30	6,744	2.9
Fasting blood glucose	Normal	128,388	55.3
	Pre-diabetic	71,372	30.8
	Diabetic	32,237	13.9
sBP	Less than 120: Healthy	82,933	35.7
	120-129: Elevated	57,366	24.7
	130=139: Stage1 hypertension	48,592	20.9
	140 or higher: Stage2 hypertension	43,106	18.6
dBP	Less than 80: Normal	156,814	67.6
	80-89: Prehypertension	55,550	23.9
	90 or higher: hypertension	19,633	8.5
Total cholesterol	Less than 200: Desirable level	143,028	61.7
	200-239: Borderline High Level	66,143	28.5
	240 and above: High level	22,826	9.8
Total		231,997	100

BMI, body mass index; sBP, systolic blood pressure; dBP, diastolic blood pressure.

observed that the HRs for urologic cancer in the high PM_{10} exposure group increased significantly after adjusting for confounding variables (P for trend < 0.001): over 56 μg/m^3 (Model 1: 1.068, 1.050-1.087; Model 2: 1.604, 1.046-1.083; Model 3: 1.604, 1.046-1.083).

We found similar results for kidney and prostate cancers (P for trend < 0.001). For kidney cancer, participants in the high PM_{10} exposure group had a higher risk than those in the low PM_{10} exposure group: over 56 μg/m^3 (Model 1: 1.122, 1,064-1.115; Model 2: 1.113, 1.070-

Table 2. Demographics according to the PM_{10} exposure

Variables		No urologic cancer			Newly developed urologic cancer		
		Low PM_{10}	High PM_{10}	*p*-value	Low PM_{10}	High PM_{10}	*p*-value
No. of patients		97,330 (100%)	83,990 (100%)	181,320	25,751 (100%)	24,926 (100%)	50,677
Age	< 65 years	41,406 (42.5)	38,708 (46.1)	0.000	18,576 (72.1)	18,520 (74.3)	0.000
	≥ 65 years	55,924 (57.5)	45,282 (53.9)		7,175 (27.9)	6,406 (25.7)	
Gender	Male	71,711 (73.7)	62,462 (74.4)	0.000	22,835 (88.7)	22,247 (89.3)	0.039
	Female	25,619 (26.3)	21,528 (25.6)		2,916 (11.3)	2,679 (10.7)	
Regular physical activity	No	52,107 (53.5)	43,077 (51.3)	0.000	10,626 (41.3)	10,231 (41.0)	0.000
	Yes: 1-4 times per week	31,087 (31.9)	28,596 (34)		11,471 (44.5)	11,533 (46.3)	
	Yes: 5 or more times per week	14,136 (14.5)	12,317 (14.7)		3,654 (14.2)	3,162 (12.7)	
Smoking	Non-smoker	61,017 (62.7)	51,203 (61)	0.000	14,822 (57.6)	13,822 (55.5)	0.000
	Ex-smoker	11,345 (11.7)	10,649 (12.7)		4,075 (15.8)	4,220 (16.9)	
	Smoker	24,968 (25.7)	22,138 (26.4)		6,854 (26.6)	6,884 (27.6)	
Alcohol consumption	No	59,228 (60.9)	49,182 (58.6)	0.000	12,149 (47.2)	11,281 (45.3)	0.000
	Yes: 2-8 times per month	23,737 (24.4)	22,545 (26.8)		9,806 (38.1)	10,058 (40.4)	
	Yes: 4 or more times per week	14,365 (14.8)	12,263 (14.6)		3,796 (14.7)	3,587 (14.4)	
Diabetes mellitus	No	84,048 (86.4)	72,219 (86)	0.023	23,829 (92.5)	23,079 (92.6)	0.000
	Yes	13,282 (13.6)	11,771 (14)		1,922 (7.5)	1,847 (7.4)	
Hypertension	No	68,976 (70.9)	58,093 (69.2)	0.000	19,775 (76.8)	19,101 (76.6)	0.817
	Yes	28,354 (29.1)	25,897 (30.8)		5,976 (23.2)	5,825 (23.4)	
BMI	25	82,896 (85.2)	71,553 (85.2)	0.000	16,272 (63.2)	15,394 (61.8)	0.001
	25-29.9	36,796 (37.8)	34,008 (40.5)		8,823 (34.3)	8,808 (35.3)	
	Over 30	3,389 (3.5)	3,355 (4)		656 (2.5)	724 (2.9)	
sBP	Less than 120: Healthy	34,474 (35.4)	28,686 (34.2)	0.000	10,113 (39.3)	9,660 (38.8)	0.000
	120-129: Elevated	23,916 (24.6)	20,272 (24.1)		6,882 (26.7)	6,296 (25.3)	
	130=139: Stage1 hypertension	20,293 (20.8)	18,002 (21.4)		5,136 (19.9)	5,161 (20.7)	
	140 or higher: Stage2 hypertension	18,647 (19.2)	17,030 (20.3)		3,620 (14.1)	3,809 (15.3)	
dBP	Less than 80: Normal	66,567 (68.4)	56,260 (67)	0.000	17,545 (68.1)	16,442 (66)	0.000
	80-89: Prehypertension	22,686 (23.3)	20,230 (24.1)		6,298 (24.5)	6,336 (25.4)	
	90 or higher: hypertension	8,077 (8.3)	7,500 (8.9)		1,908 (7.4)	2,148 (8.6)	
Fasting blood sugar	Normal	52,389 (53.8)	45,635 (54.3)	0.078	15,367 (59.7)	14,997 (60.2)	0.093
	Pre diabetic	30,211 (31)	25,702 (30.6)		7,846 (30.5)	7,613 (30.5)	
	Diabetic (125 or higher)	14,730 (15.1)	12653 (15.1)		2,538 (9.9)	2,316 (9.3)	
Total Cholesterol (mg/dL)	Less than 200: Desirable level	61,110 (62.8)	51715 (61.6)	0.000	15,462 (60)	14,741 (59.1)	0.093
	200-239: Borderline High Level	26,690 (27.4)	23856 (28.4)		7,818 (30.4)	7,779 (31.2)	
	240 and above: High level	9,530 (9.8)	8419 (10)		2,471 (9.6)	2,406 (9.7)	

BMI, body mass index; sBP, systolic blood pressure; dBP, diastolic blood pressure.

Table 3. Hazard ratios of urologic cancer according to the PM_{10} exposure

Cancer	PM_{10} concentration (unit: μg/m³)	Event	Person-years	Incidence rate[a]	HR (95% CI)		
					Model 1[b]	Model 2[c]	Model 3[d]
Urologic cancer (N=50,677, 100%)	< 56	25,751	799,101	32.225	1 (ref.)	1 (ref.)	1 (ref.)
	≥ 56	24,926	706,259	35.293	1.068 (1.050, 1.087)	1.064 (1.046, 1.083)	1.064 (1.046, 1.083)
		P for trend			< 0.001	< 0.001	< 0.001
Kidney cancer (N=9,736, 19.2%)	< 56	4,817	660,560	7.292	1 (ref.)	1 (ref.)	1 (ref.)
	≥ 56	4,919	573,552	8.576	1.122 (1.064, 1.115)	1.113 (1.070, 1.158)	1.111 (1.068, 1.157)
		P for trend			< 0.001	< 0.001	< 0.001
Prostate cancer (N=28,440, 56.1%)	< 56	14,379	560,576	25.650	1 (ref.)	1 (ref.)	1 (ref.)
	≥ 56	14,061	496,225	28.336	1.089 (1.064, 1.115)	1.083 (1.058, 1.108)	1.083 (1.058, 1.109)
		P for trend			< 0.001	< 0.001	< 0.001
Urothelial cancer (N=12,501, 24.7%)	< 56	6,555	671,750	9.758	1 (ref.)	1 (ref.)	1 (ref.)
	≥ 56	5,946	579,292	10.264	1.032 (0.996, 1.069)	1.027 (0.992, 1.064)	1.029 (0.993, 1.066)
		P for trend			n.s	n.s	n.s

[a]Incidence per 1,000 person-years. [b]Model 1 was adjusted for age and gender. [c]Model 2 was adjusted for age, gender, regular activity smoking status, and alcohol consumption. [d]Model 3 was adjusted for age, gender, regular activity, smoking status, alcohol consumption, diabetes mellitus, and hypertension. HR, hazard ratio; CI, confidence interval.

1.158; Model 3: 1.111, 1.068-1.157). For prostate cancer, participants in the high PM_{10} exposure group had a higher risk than those in the low PM_{10} exposure group: over 56 μg/m^3 (Model 1: 1.089, 1.064-1.115; Model 2: 1.083, 1.058-1.108; Model 3: 1.083, 1.058-1.109). However, in urothelial cell carcinoma, there was no significant increase in the HRs in the high PM_{10} exposure group.

Risk of urologic cancer in clinically relevant subgroup

We conducted subgroup analysis based on several clinically relevant variables (**Table 4**). We observed the same trend of increasing risk of kidney and prostate cancer in participants in the high PM_{10} group compared with those in the low PM_{10} group. For kidney cancer, participants with the following characteristics were more susceptible to these associations: age < 65 years, female sex, decreased regular physical activity, current smoking, no DM, no hypertension, normal BMI, and desirable total cholesterol level. For prostate cancer, participants with the following characteristics were more susceptible to these associations: decreased regular physical activity, current smoking, and no hypertension.

Discussion

Considering the rapidly urbanizing world, it is becoming increasingly important to evaluate air pollution as a determinant of cancer, especially with respect to the reduction of some traditional risk factors, such as smoking, workplace carcinogens, and solid fuel, which may be improved over time with various smoking control activities, workplace safety measures, and socioeconomic development. In this respect, there were several important observations in our study regarding the association of urologic cancer and PM_{10} exposure. We found that high PM_{10} exposure was associated with an increased risk of overall urologic cancer, especially kidney and prostate cancers. We also found that the increased risk of kidney and prostate cancer related to high PM_{10} exposure was significantly augmented among participants with current smoking, female sex (only in kidney cancer), and no features of metabolic disorders, and decreased among participants with regular physical activity five or more times per week.

Currently available studies on the association between the risk of urologic cancer and air pollution have reported conflicting results. Fourteen cohorts from the European Study of Cohorts for Air Pollution Effects study demonstrated higher HRs for kidney parenchyma cancer in association with higher $PM_{2.5}$ concentrations (HRs 1.57, 95% CI 0.81-3.01, per 5 μg/m^3 $PM_{2.5}$), although not statistically significant [22]. In a population-based study in Shanghai, China, waste gas emissions were positively associated with multiple cancers, incidence including kidney, bladder, and prostate cancer [23]. In a recent Canadian case-control study, positive associations were found between exposure to $PM_{2.5}$ and NO_2 over the previous 20 years and prostate cancer [24]. However, a Danish cohort study that investigated the association between NO_2 and 20 selected cancers reported an association between NO_2 exposure and increased risk of cervical and brain cancer but not with bladder, kidney, and prostate cancer [25]. Thus, a recent systematic review of 20 studies concluded that most previous studies reported a positive association between air pollution and bladder or kidney cancer risk, but only a few reached statistical significance; also most studies inadequately addressed confounding factors, and cohort studies had insufficient numbers of participants and follow-up duration [15]. Our study is meaningful in that it presents positive results using a large number of participants, after controlling for sufficient confounding factors.

One of the interesting details of our study is that the impact of PM_{10} exposure on subsequent kidney and prostate cancer risks was more prominent in participants with specific characteristics. First, the association between PM_{10} exposure and risk of kidney cancer was more prominent in females than males. It is not clear whether females are more susceptible to cancers associated with air pollution. Similar to our findings, Li et al. reported that females were more susceptible to the association between the risk of esophageal cancer and air pollution than males [26]. Although it is not a cancer research, Liu et al. also reported that susceptibility to cardiovascular mortality from air pollution was higher among females than males [27]. Further researches on the difference in urologic cancer susceptibility from air pollution in males and females is needed.

Table 4. Hazard ratios (95% CI) of urologic cancer according to the PM_{10} exposure in clinically relevant subgroups

Variables	Kidney cancer		Prostate cancer	
	Low PM_{10}	High PM_{10}	Low PM_{10}	High PM_{10}
	< 56 μg/m³	≥ 56 μg/m³	< 56 μg/m³	≥ 56 μg/m³
Age				
< 65 years	1 (ref.)	1.135 (1.088, 1.185)***	1 (ref.)	1.077 (1.048, 1.108)***
≥ 65 years	1 (ref.)	1.051 (0.943, 1.173)	1 (ref.)	1.119 (1.072, 1.168)***
Gender				
Male	1 (ref.)	1.176 (1.122, 1.233)***	1 (ref.)	1.118 (1.093, 1.145)***
Female	1 (ref.)	1.214 (1.128, 1.306)***		
Regular physical activity				
No	1 (ref.)	1.300 (1.224, 1.381)***	1 (ref.)	1.146 (1.104, 1.189)***
Yes: 1-4 times per week	1 (ref.)	1.083 (1.021, 1.148)**	1 (ref.)	1.104 (1.067, 1.142)***
Yes: 5 or more times per week	1 (ref.)	1.084 (0.958, 1.226)	1 (ref.)	1.021 (0.960, 1.085)
Alcohol consumption				
No	1 (ref.)	1.183 (1.117, 1.252)***	1 (ref.)	1.113 (1.075, 1.153)***
Yes: 2-8 times per month	1 (ref.)	1.148 (1.079, 1.221)***	1 (ref.)	1.114 (1.074, 1.156)***
Yes: 4 or more times per week	1 (ref.)	1.182 (1.049, 1.331)**	1 (ref.)	1.085 (1.023, 1.151)**
Smoking				
Non-smoker	1 (ref.)	1.177 (1.118, 1.240)***	1 (ref.)	1.094 (1.061, 1.129)***
Ex-smoker	1 (ref.)	1.116 (0.996, 1.250)*	1 (ref.)	1.129 (1.070, 1.191)***
Smoker	1 (ref.)	1.238 (1.149, 1.333)***	1 (ref.)	1.164 (1.111, 1.220)***
Diabetes mellitus				
No	1 (ref.)	1.196 (1.147, 1.246)***	1 (ref.)	1.117 (1.090, 1.144)***
Yes	1 (ref.)	1.097 (0.939, 1.282)	1 (ref.)	1.147 (1.052, 1.251)**
Hypertension				
No	1 (ref.)	1.227 (1.174, 1.284)***	1 (ref.)	1.138 (1.108, 1.169)***
Yes	1 (ref.)	1.087 (0.998, 1.185)*	1 (ref.)	1.075 (1.025, 1.127)**
BMI				
25	1 (ref.)	1.207 (1.144, 1.273)***	1 (ref.)	1.127 (1.095, 1.161)***
25-29.9	1 (ref.)	1.142 (1.072, 1.217)***	1 (ref.)	1.086 (1.044, 1.130)***
Over 30	1 (ref.)	1.130 (0.948, 1.347)	1 (ref.)	1.192 (1.006, 1.411)**
Fasting blood sugar				
Normal	1 (ref.)	1.204 (1.145, 1.266)***	1 (ref.)	1.113 (1.080, 1.147)
Pre diabetic	1 (ref.)	1.197 (1.111, 1.289)***	1 (ref.)	1.131 (1.085, 1.179)
Diabetic (125 or higher)	1 (ref.)	1.026 (0.898, 1.173)	1 (ref.)	1.100 (1.020, 1.187)
Total cholesterol				
Less than 200: Desirable level	1 (ref.)	1.244 (1.181, 1.311)***	1 (ref.)	1.119 (1.086, 1.153)***
200-239: Borderline High Level	1 (ref.)	1.119 (1.042, 1.201)**	1 (ref.)	1.108 (1.063, 1.156)***
240 and above: High level	1 (ref.)	1.061 (0.940, 1.198)	1 (ref.)	1.104 (1.021, 1.194)**

HR, hazard ratio; CI, confidence interval. HRs (95% CIs) were obtained using multivariable Cox proportional hazard regression analysis after adjusting age, gender, regular physical activity, alcohol consumption, smoking, diabetes mellitus, hypertension, BMI, fasting blood sugar, and total cholesterol. *$P < 0.05$; **$P < 0.01$; ***$P < 0.001$.

Second, the association between PM_{10} exposure and the risk of kidney and prostate cancers was more prominent in participants without features of metabolic disorders. The rationale for these results is unclear. However, it is necessary to consider that metabolic disorders such as DM, hypertension, and dyslipidemia are important risk factors for urologic cancer. A recent meta-analysis of 151 cohort studies comprising 32 million participants showed that

DM was associated with an increased risk of kidney (pooled relative risk [RR] 1.32, 95% CI 1.21-1.44) and bladder (pooled RR 1.19, 95% CI 1.09-1.29) cancer [28]. Another meta-analysis of 24 studies including a total of 132,589 participants reported an association between metabolic syndrome and prostate cancer incidence (odds ratio [OR] 1.17, 95% CI 1.00-1.36) and between metabolic syndrome and high-grade prostate cancer (OR 1.89, 95% CI 1.50-2.38) [29]. Considering the well-known mechanisms linking DM, hypertension, and dyslipidemia to cancer [30-32], it can be assumed that the risk of urologic cancer did not increase as similar mechanisms of these chronic diseases and PM_{10} are complementary.

Finally, the association between PM_{10} concentration and the risks of both kidney and prostate cancers differed according to the category of regular physical activity. In participants with no regular physical activity or regular physical activity 1-4 times per week, high PM_{10} exposure was significantly associated with increased risks of kidney and prostate cancer. In contrast, in participants who engaged in regular physical activity five or more times per week, high PM_{10} exposure was not associated with an increased risk of kidney and prostate cancer. Although regular physical activity is known to reduce the incidence and mortality from cardiovascular diseases, type 2 DM, and several cancers [33, 34], there might be some concerns regarding exposure to air pollution during physical activity. However, numerous epidemiological and modeling studies have suggested that the long-term benefits of physical activity in urban areas outweigh the risks of exposure to air pollution [35]. The results of our study might provide additional evidence that regular physical activity offsets the risks of kidney and prostate cancer associated with PM_{10} exposure.

This study had some limitations. First, we excluded participants who did not undergo more than four consecutive health examinations from 2010 to 2018 to avoid the bias of cancer not being diagnosed, even though it has actually occurred. However, the risk of another selection bias may have occurred because a significant number of participants who did not receive more than four consecutive health examinations were excluded. Second, we estimated the level of individual exposure to PM_{10} by using fixed outdoor measurement stations near their residential regions. This approach may ignore the possible differences between individuals within the same residential region with regard to occupational exposure, daily activity area, indoor or outdoor exposure time, and the use of air purifiers. However, previous studies have shown that personal PM concentrations correlate reasonably well with PM concentrations measured at fixed outdoor measuring stations [36]. Finally, in 2008, the level of air pollution in South Korea was less severe than it is now, and the distribution or number of measurements of air pollutants was not as large as it is now. Therefore, this should be considered when interpreting our results. However, the major strength of our study was its large sample size, which allowed us to comprehensively control for important confounding factors.

Conclusions

High PM_{10} exposure is associated with an increased risk of overall urologic cancer, especially kidney and prostate cancers. Additionally, the increased risk of kidney and prostate cancer related to high PM_{10} exposure is significantly increased by current smoking, female sex (only in kidney cancer), and no features of metabolic disorders, and is decreased with regular physical activity five or more times a week. Although further studies are needed, physicians should consider more attentive lifestyle interventions, including air quality improvement and encouraging regular physical activity, to decrease the risk of urological cancers.

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Disclosure of conflict of interest

Mi Jung Rho and Jihwan Park are married couples and are part of Dankook University, co-participating in the project. None of the contributing authors has any conflicts of interest, including specific financial interests, relationships, or affiliations relevant to the subject matter or materials discussed in the manuscript.

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