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Association between air pollution exposure and lower urinary tract symptoms in Korean men

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The purpose of this study was to investigate the association between long-term air pollution exposure and Low Urinary Tract Symptoms (LUTS) in Korean men. This study included 7,979 adult men who underwent health checkups. Each subject's annual average air pollution exposure levels were estimated using the *Community Multiscale Air Quality* model. LUTS were evaluated using the *International Prostate Symptom Score* (IPSS) questionnaire, and the IPSS values were analyzed for their association with LUTS severity. The study population had an average age of 56.1 years, with a prevalence of LUTS at 39.8%. None of the air pollutants were significantly associated with overall LUTS prevalence after adjusting for potential confounders. Interestingly, when divided into two symptoms of LUTS, exposures to particulate matter ≤ 2.5 μm in diameter ($PM_{2.5}$) and particulate matter ≤ 10 μm in diameter (PM_{10}) were significantly associated with an increased prevalence of voiding symptoms, but not with storage symptoms. Regarding the LUTS severity, $PM_{2.5}$ and sulfur dioxide (SO_2) exposures were closely related to an increased severity of overall LUTS. We report for the first time that long-term exposure to ambient air pollution, such as particulate matter, is associated with a higher prevalence and severity of LUTS, particularly voiding symptoms.

Keywords Air pollution, Low urinary tract symptoms, Particulate matter, Sulfur dioxide, Carbon monoxide, Ozone

Lower urinary tract symptoms (LUTS) have an adverse impact on the quality of life of elderly men[1]. With the ongoing aging of the global population, the burden of LUTS is increasing in most of the world[2]. In South Korea, the LUTS prevalence is also high at 44.7% among men aged > 40 years, and this prevalence shows a marked increase with advanced age[3]. Therefore, the risk factors for LUTS must be clarified for its prevention and management. Although age, obesity, smoking, and metabolic syndrome[4,5] are known risk factors of LUTS, the role of environmental factors, including air pollution, needs to be elucidated.

Air pollution adversely impacts multiple organ systems, including respiratory, cardiovascular, endocrine, neurological, urological, and digestive system[6–8]. These impacts affect both short- and long-term health outcomes. Inflammatory responses and neuroendocrine dysregulation are the shared biological mechanisms underlying the association between air pollution and various diseases. Moreover, LUTS is also influenced by chronic inflammation of the prostatic tissue and neuroendocrine dysregulation of the sympathetic and parasympathetic nervous systems affecting the bladder and urethra[9–12]. Within this context, it is reasonable to speculate that there could be an association between air pollution and LUTS, given the common pathogenesis mentioned above. Until now, several studies have documented a correlation between air pollution and prostate cancer. However, to the best of our knowledge, no study has identified the association between air pollution and LUTS.

Therefore, the objective of this study was to explore the correlation between long-term air pollution exposure and the prevalence and severity of LUTS in Korean men. We also divided the LUTS into two categories according to their symptoms (i.e., voiding and storage symptoms) and assessed their relationship with ambient air pollution.

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Results

Table 1 presents the general characteristics of the 7,979 study subjects. The mean age of the total sample was 56.1 years, and the prevalence of LUTS was 39.8%. The mean age of the population with LUTS was 58.6, which was higher than that of the population without LUTS (54.4 years). Individuals with LUTS exhibited lower BMI, higher PSA levels, lower alcohol consumption, and higher long-term smoking history than those without LUTS (all $p < 0.05$). Compared to the group without LUTS, the prevalence of diabetes and hypertension was higher in the group with moderate-to-severe LUTS (both $p < 0.05$). In contrast, the prevalence of dyslipidemia was lower in individuals with LUTS (52.5%) than in those without LUTS (54.8%) ($p = 0.040$). For ambient air pollutants, the annual mean values of $PM_{2.5}$ exposure concentration were similar between the LUTS and non-LUTS groups ($p = 0.292$). In the O_3 exposure group, the LUTS group had a higher exposure level than the non-LUTS group ($p < 0.001$). In contrast, in the LUTS group, the annual mean values of other air pollutants, including PM_{10}, NO_2, SO_2, and CO, were lower compared to the non-LUTS group (all $p < 0.05$).

The mean and median annual concentrations of each air pollutant are presented in (Supplementary Table A). The means of $PM_{2.5}$, PM_{10}, NO_2, SO_2, CO, and O_3 were 24.5 μg/m^3, 44.6 μg/m^3, 26.4 ppb, 4.2 ppb, 504.2 ppb, and 25.9 ppb, respectively, and the IQRs for $PM_{2.5}$, PM_{10}, NO_2, SO_2, CO and O_3 were 2.6 μg/m^3, 6.9 μg/m^3, 14.3 ppb,

Characteristics	LUTS		Total	*p*-value
	None-mild	Moderate-severe		
Total, No. (%)	4803 (60.2)	3176 (39.8)	7979 (100)	
Age (years), mean ± SD	54.4 ± 10.5	58.6 ± 10.5	56.1 ± 10.7	< 0.001
BMI (kg/m^2), mean ± SD	24.6 ± 3.0	24.4 ± 3.0	24.5 ± 3.0	0.009
PSA (ng/mL), mean ± SD	1.1 ± 1.1	1.3 ± 1.3	1.2 ± 1.2	< 0.001
Age group, No. (%)				< 0.001
30–39	520 (10.8)	163 (5.1)	683 (8.6)	
40–49	990 (20.6)	451 (14.2)	1441 (18.1)	
50–59	1718 (35.8)	1037 (32.7)	2755 (34.5)	
60–69	1242 (25.9)	1054 (33.2)	2296 (28.8)	
≥ 70	333 (6.9)	471 (14.8)	804 (10.1)	
Smoking, No. (%)				< 0.001
Never smoker	1159 (24.1)	634 (20.0)	1793 (22.5)	
Ex-smoker	2206 (45.9)	1607 (50.6)	3813 (47.8)	
Current smoker	1438 (29.9)	935 (29.4)	2373 (29.7)	
Alcohol, No. (%)				0.003
None	1311 (27.3)	975 (30.7)	2286 (28.7)	
> 0 and ≤ 2 drinks/day	2113 (44.0)	1303 (41.0)	3416 (42.8)	
> 2 drinks/day	1379 (28.7)	898 (28.3)	2277 (28.5)	
Diabetes, No. (%)				< 0.001
No	4021 (83.7)	2513 (79.1)	6534 (81.9)	
Yes	782 (16.3)	663 (20.9)	1445 (18.1)	
Hypertension, No. (%)				0.005
No	2935 (61.1)	1841 (58.0)	4776 (59.9)	
Yes	1868 (38.9)	1335 (42.0)	3203 (40.1)	
Dyslipidemia, No. (%)				0.040
No	2171 (45.2)	1510 (47.5)	3681 (46.1)	
Yes	2632 (54.8)	1666 (52.5)	4298 (53.9)	
Air pollution (annual average concentration)				
$PM_{2.5}$ (μm/m^3), mean ± SD	24.5 ± 2.5	24.5 ± 2.7	24.5 ± 2.6	0.292
PM_{10} (μm/m^3), mean ± SD	44.7 ± 5.2	44.5 ± 5.4	44.6 ± 5.3	0.026
NO_2 (ppb), mean ± SD	26.8 ± 8.9	25.9 ± 9.0	26.4 ± 8.9	< 0.001
SO_2 (ppb), mean ± SD	4.2 ± 0.9	4.2 ± 0.9	4.2 ± 0.9	0.044
CO (ppb), mean ± SD	507.2 ± 69.3	499.5 ± 73.7	504.2 ± 71.2	< 0.001
O3 (ppb), mean ± SD	25.7 ± 5.1	26.2 ± 5.4	25.9 ± 5.2	< 0.001

Table 1. Characteristics of study participants. *SD* standard deviation, *BMI* body mass index, *PSA* prostate-specific antigen, *MET* Metabolic Equivalent Task, $PM_{2.5}$ particulate matter ≤ 2.5 μm in diameter, PM_{10} particulate matter ≤ 10 μm in diameter, NO_2 nitrogen dioxide, SO_2 sulfur dioxide, *CO* carbon monoxide, O_3 ozone; Continuous variables are presented as mean ± SD, while categorical variables are presented as No. (%). The p-value was calculated by Chi-squared test for categorical variables and Student's *t*-test for continuous variables.

Air pollutants	Moderate-severe LUTS			
	Unadjusted		Adjusted	
	OR (95% CI)	*p*-value	OR (95% CI)	*p*-value
$PM_{2.5}$ (μg/m^3)	0.98 (0.93, 1.02)	0.292	1.06 (1.00, 1.11)	0.053
PM_{10} (μg/m^3)	**0.94 (0.88, 0.99)**	**0.026**	1.05 (0.97, 1.13)	0.216
NO_2 (ppb)	**0.86 (0.80, 0.92)**	**< 0.001**	1.02 (0.85, 1.23)	0.802
SO_2 (ppb)	**0.95 (0.89, 1.00)**	**0.044**	1.06 (0.99, 1.13)	0.120
CO (ppb)	**0.87 (0.82, 0.92)**	**< 0.001**	0.94 (0.84, 1.04)	0.233

Table 2. The association between ambient air pollution and the prevalence of moderate-severe lower urinary tract symptoms. *LUTS* lower urinary tract symptoms, *$PM_{2.5}$* particulate matter ≤ 2.5 μm in diameter, *PM_{10}* particulate matter ≤ 10 μm in diameter, *NO_2* nitrogen dioxide, *SO_2* sulfur dioxide, *CO* carbon monoxide, *OR* odds ratio, *CI* confidence interval. The ORs and 95% CIs of air pollutants were adjusted based on the interquartile range (IQR) of each pollutant: 3 μg/m^3 for $PM_{2.5}$, 7 μg/m^3 for PM_{10}, 14 ppb for NO_2, 1 ppb for SO_2 and 90 ppb for CO. In the adjusted model, the data were controlled for age, hypertension, dyslipidemia, diabetes, body mass index, smoking status ("never smoked", "former smoker", or "current smoker"), daily alcohol consumption ("non-drinking", "less than two drinks", or "two or more drinks" per day), prostate-specific antigen, and ozone exposure. Significant values are in bold.

Air pollutants	Moderate-severe voiding symptoms				Moderate-severe storage symptoms			
	Unadjusted model		Adjusted model		Unadjusted model		Adjusted model	
	OR (95% CI)	*p*-value	OR (95% CI)	*p*-value	OR (95% CI)	*p*-value	OR (95% CI)	*p*-value
$PM_{2.5}$ (μg/m^3)	0.99 (0.95, 1.04)	0.687	**1.08 (1.02, 1.14)**	**0.009**	0.97 (0.93, 1.02)	0.230	1.03 (0.98, 1.09)	0.234
PM_{10} (μg/m^3)	0.96 (0.90, 1.01)	0.127	**1.08 (1.00, 1.16)**	**0.049**	**0.93 (0.88, 0.99)**	**0.022**	1.02 (0.95, 1.10)	0.607
NO_2 (ppb)	**0.86 (0.80, 0.93)**	**< 0.001**	1.04 (0.86, 1.26)	0.675	**0.88 (0.81, 0.94)**	**< 0.001**	1.00 (0.83, 1.21)	0.974
SO_2 (ppb)	0.96 (0.90, 1.01)	0.112	1.07 (1.00, 1.15)	0.053	0.95 (0.90, 1.00)	0.069	1.04 (0.97, 1.12)	0.255
CO (ppb)	**0.88 (0.83, 0.93)**	**< 0.001**	0.93 (0.84, 1.04)	0.220	**0.91 (0.86, 0.96)**	**0.001**	1.00 (0.90, 1.12)	0.949

Table 3. The association between ambient air pollution and the prevalence of moderate-severe lower urinary tract symptoms, stratified by voiding and storage subgroup. *LUTS* lower urinary tract symptoms, *$PM_{2.5}$* particulate matter ≤ 2.5 μm in diameter, *PM_{10}* particulate matter ≤ 10 μm in diameter, *NO_2* nitrogen dioxide, *SO_2* sulfur dioxide, *CO* carbon monoxide, *OR* odds ratio, *CI* confidence interval. The ORs and 95% CIs of air pollutants were adjusted based on the interquartile range (IQR) of each pollutant: 3 μg/m^3 for $PM_{2.5}$, 7 μg/m^3 for PM_{10}, 14 ppb for NO_2, 1 ppb for SO_2 and 90 ppb for CO. In the adjusted model, the data were controlled for age, hypertension, dyslipidemia, diabetes, body mass index, smoking status ("never smoked", "former smoker", or "current smoker"), daily alcohol consumption ("non-drinking", "less than two drinks", or "two or more drinks" per day), prostate-specific antigen, and ozone exposure. Significant values are in bold.

1.1 ppb, 90.1 ppb and 6.8 ppb, respectively. There were significant positive correlations between all air pollutants except for O_3, whereas O_3 was significantly and negatively correlated with all other air pollutants (all $p < 0.05$).

Tables 2 and 3 show the association of air pollution with the prevalence of LUTS and subgroups categorized by symptoms. The results are presented in both the crude and adjusted models. In the adjusted model, variables that were significant between the LUTS and non-LUTS groups as shown in (Table 1) were finally included as confounding factors. We also considered O_3 as a covariate in the adjusted model. This is because O_3 showed an opposite pattern to the other air pollutants (Table 1), which may cause confounding in the association between other air pollutants and LUTS.

As shown in Table 2, $PM_{2.5}$ exposure did not show a significant association with LUTS in the crude model, but a marginal association was found in the adjusted model (OR = 1.06; 95% CI = 1.00–1.11). Other air pollutants, including PM_{10}, NO_2, SO_2, and CO, showed a negative correlation with the risk of moderate-to-severe LUTS in the crude model (all $p < 0.05$). However, after adjusting for confounding factors, all statistically significant associations between these air pollutants and LUTS disappeared (all $p > 0.05$). The association results stratified by the voiding and storage subgroups of LUTS are presented in Table 3. In an adjustment model, exposures to both $PM_{2.5}$ (OR = 1.08; 95% CI = 1.02–1.14) and PM_{10} (OR = 1.08; 95% CI = 1.00–1.16) showed significant associations with a higher prevalence of voiding LUTS. No associations were observed between voiding LUTS and other air pollutants (all $p > 0.05$). Moreover, none of the air pollutants were closely related to storage LUTS after adjusting for potential confounders (all $p > 0.05$).

Table 4 shows the association between air pollutant exposure and the overall severity of LUTS. The $PM_{2.5}$ ($\beta = 0.23$; 95% CI = 0.06–0.40) and SO_2 ($\beta = 0.31$; 95% CI = 0.09–053) concentrations were significantly associated with the total IPSS level. For other air pollutants, significant inverse associations with the total IPSS were found in the crude model (all $p < 0.05$), but their effects were not maintained in the adjusted model (all $p > 0.05$). The results of the association divided by the two symptoms of LUTS (i.e., voiding and storage symptoms) are provided

Air pollutants	IPSS-score			
	Unadjusted		Adjusted	
	β (95% CI)	*p*-value	β (95% CI)	*p*-value
$PM_{2.5}$ (μg/m^3)	−0.08 (−0.24, 0.07)	0.277	**0.23 (0.06, 0.40)**	**0.008**
PM_{10} (μg/m^3)	**−0.24 (−0.44, −0.05)**	**0.015**	0.23 (−0.00, 0.47)	0.052
NO_2 (ppb)	**−0.62 (−0.86, −0.38)**	**<0.001**	0.29 (−0.31, 0.88)	0.345
SO_2 (ppb)	−0.17 (−0.35, 0.01)	0.071	**0.31 (0.09, 0.53)**	**0.005**
CO (ppb)	**−0.49 (−0.68, −0.30)**	**<0.001**	0.02 (−0.33, 0.36)	0.919

Table 4. The association between ambient air pollution and the severity of lower urinary tract symptoms. *IPSS* International Prostatism Symptom Score, $PM_{2.5}$ particulate matter ≤ 2.5 μm in diameter, PM_{10} particulate matter ≤ 10 μm in diameter, NO_2 nitrogen dioxide, SO_2 sulfur dioxide, *CO* carbon monoxide, *CI* confidence interval. The beta coefficients and 95% CIs of air pollutants were adjusted based on the interquartile range (IQR) of each pollutant: 3 μg/m^3 for $PM_{2.5}$, 7 μg/m^3 for PM_{10}, 14 ppb for NO_2, 1 ppb for SO_2 and 90 ppb for CO. In the adjusted model, the data were controlled for age, hypertension, dyslipidemia, diabetes, body mass index, smoking status ("never smoked", "former smoker", or "current smoker"), daily alcohol consumption ("non-drinking", "less than two drinks", or "two or more drinks" per day), prostate-specific antigen, and ozone exposure. Significant values are in bold.

Air pollutants	IPSS-score (voiding symptoms)				IPSS-score (storage symptoms)			
	Unadjusted model		Adjusted model		Unadjusted model		Adjusted model	
	β (95% CI)	*p*-value	β (95% CI)	*p*-value	β (95% CI)	*p*-value	β (95% CI)	*p*-value
$PM_{2.5}$ (μg/m^3)	−0.04 (−0.15, 0.06)	0.445	**0.17 (0.05, 0.29)**	**0.005**	−0.04 (−0.11, 0.02)	0.180	0.06 (−0.01, 0.13)	0.109
PM_{10} (μg/m^3)	**−0.15 (−0.29, −0.02)**	**0.027**	0.16 (−0.00, 0.32)	0.054	**−0.09 (−0.17, −0.01)**	**0.030**	0.07 (−0.03, 0.17)	0.149
NO_2 (ppb)	**−0.40 (−0.56, −0.23)**	**<0.001**	0.24 (−0.17, 0.65)	0.257	**−0.22 (−0.32, −0.12)**	**<0.001**	0.05 (−0.20, 0.30)	0.707
SO_2 (ppb)	−0.10 (−0.23, 0.02)	0.114	**0.22 (0.06, 0.37)**	**0.005**	−0.07 (−0.14, 0.01)	0.086	**0.10 (0.01, 0.19)**	**0.037**
CO (ppb)	**−0.32 (−0.45, −0.19)**	**<0.001**	0.02 (−0.21, 0.26)	0.845	**−0.17 (−0.25, −0.09)**	**<0.001**	−0.01 (−0.15, 0.14)	0.936

Table 5. The association between ambient air pollution and the severity of lower urinary tract symptoms, stratified by voiding and storage subgroup. *IPSS* International Prostatism Symptom Score, $PM_{2.5}$ particulate matter ≤ 2.5 μm in diameter, PM_{10} particulate matter ≤ 10 μm in diameter, NO_2 nitrogen dioxide, SO_2 sulfur dioxide, *CO* carbon monoxide, *CI* confidence interval. The beta coefficients and 95% CIs of air pollutants were adjusted based on the interquartile range (IQR) of each pollutant: 3 μg/m^3 for $PM_{2.5}$, 7 μg/m^3 for PM_{10}, 14 ppb for NO_2, 1 ppb for SO_2 and 90 ppb for CO. In the adjusted model, the data were controlled for age, hypertension, dyslipidemia, diabetes, body mass index, smoking status ("never smoked", "former smoker", or "current smoker"), daily alcohol consumption ("non-drinking", "less than two drinks", or "two or more drinks" per day), prostate-specific antigen, and ozone exposure. Significant values are in bold.

in Table 5. The results for the severity of voiding symptom were similar to those for severity of overall LUTS, showing the significant association between exposure to $PM_{2.5}$ ($\beta = 0.17$; 95% CI = 0.05–0.29) or SO_2 ($\beta = 0.22$; 95% CI = 0.06–037) and IPSS level for voiding symptoms. However, in the results for the severity of storage symptom, only SO_2 exposure was observed to be associated with IPSS level ($\beta = 0.10$; 95% CI = 0.01–0.19).

Discussion

This study examined the relationship between long-term exposure to air pollutants and the prevalence and severity of LUTS in Korean men. We found that the annual average concentrations of $PM_{2.5}$ and PM_{10} were associated with an increased prevalence of voiding symptoms. Specifically, $PM_{2.5}$ was also related to the severity of overall and voiding symptoms. In addition, exposure to SO_2 was notably linked to the severity of overall, voiding and storage LUTS.

Although no studies have investigated the relationship between exposure to air pollution and LUTS, numerous studies have identified various risk factors for LUTS. For instance, Choo et al. reported that smoking and low physical activity are associated with increased incidence of LUTS[13], and Penson et al. revealed that obesity is an important risk factor for LUTS[14]. Moreover, metabolic syndrome and related disorders, including diabetes mellitus and hypertension, lead to the development of LUTS[4]. Emerging evidence from studies based on animal models and humans has shown that long-term exposure to air pollution leads to the development of metabolic syndrome-related diseases, via systemic inflammatory responses[15]. In this context, metabolic syndrome-related diseases may mediate air pollution-induced LUTS.

Nevertheless, our study results revealed notable associations between these air pollutants and LUTS, even after controlling for confounding variables such as lifestyle, BMI, and underlying diseases. The observed differences in the associations between air pollutants in unadjusted and adjusted models may be explained by

variations in the residential areas of the population. Younger individuals are more likely to live in urban areas with higher levels of air pollution, whereas older individuals tend to reside in rural areas with lower pollution. Since age is a strong risk factor for LUTS, this demographic distribution could result in a higher prevalence of LUTS in older populations from low-pollution areas, even if the difference is not statistically significant. Adjusting for confounding factors, such as age and chronic diseases, thus helps to better elucidate the true relationship between air pollution and LUTS.

This indicates a direct link between air pollution exposure and an elevated risk of LUTS, in addition to the possibility of the aforementioned mediating effect. Particulate matter has the potential to increase the generation of reactive oxygen species and activated various inflammatory pathways, cytokines, and gene expressions responsible for inflammation-mediated damage[16]. Oxidative stress triggers a sequence of cellular responses involving the activation of kinase cascades and transcription factors, as well as the release of inflammatory mediators[17]. Previous studies have proposed that immuno-inflammatory stimulators can influence the growth of prostatic epithelial cells by regulating the cytokine system, potentially leading to hyperplastic alterations[18] that induce voiding symptoms. Moreover, oxidative stress and systemic inflammation can induce metabolic issues, including endothelial dysfunction and insulin resistance. These can accelerate atherosclerosis and pelvic ischemia, potentially leading to change in the function and structure of the detrusor[19]. Additionally, metabolic syndrome induced by particulate matter can cause the formation of inflammatory infiltrates within the prostate, resulting in prostate enlargement and increased autonomic nervous system activity, contributing to detrusor muscle contraction[20,21]. In particulate matter-induced obesity, adipocytes may directly contribute to prostate enlargement by expressing aromatase, leading to alterations in sex steroid levels and influencing LUTS through the release of cytokines and the provocation of an inflammatory response, ultimately inducing metabolic syndrome. SO_2 exposure appeared to have a similar effect to particulate matter.

In our study, the results of the association between ambient air pollution and LUTS differed depending on the two symptoms, and a significant association was mainly found with voiding symptoms. This can be attributed to the mechanism of occurrence of each symptom. LUTS refer to a term encompasses a variety of symptoms associated with the lower urinary tract, which can be categorized as either voiding or storage symptoms based on urinary tract function. Voiding symptoms are usually affected by obstruction of urinary function, which is mainly attributed to prostate enlargement and increased smooth muscle tone in the prostatic stroma, whereas storage symptoms are often affected by impaired bladder function associated with detrusor overactivity[9]. Although the potential mechanisms discussed above may have an impact on both voiding and storage LUTS, particulate matter primarily directly affects the inflammatory pathway that induces prostate hyperplasia, thereby leading to voiding symptoms. Therefore, further studies on the potential mechanism, including the association between exposure to particulate matter and prostate volume, are required.

As far as we know, this is the first study to report that long-term exposure to ambient air pollution is closely related to an increased prevalence and severity of LUTS. Our study used CMAQ modeling data based on observational data to evaluate individual air pollution exposure levels. This method is more accurate than relying on the estimates from nearby monitoring stations. However, this study had some limitations that need to be considered. First, individual exposure levels were estimated using the participants' residential addresses, which did not account for their relocations, working areas duration of outdoor activity, or indoor air quality. Indeed, it is very difficult to collect accurate data on individual movements, especially in large-scale epidemiological studies. For this reason, we could not consider various factors such as how much time they spent outdoors or how long it took them to commute to work, in addition to their movement history. Second, we could not control for all potential confounding variables known to be associated with LUTS, such as depression[4,5,22] and caffeine[4,23], because to the absence of relevant data. Third, this study used self-reported data to evaluate LUTS, which may have been inaccurate. Finally, a cross-sectional design was employed. Therefore, we are unable to make causal conclusions about the connection between ambient air pollution and LUTS.

Long-term exposure to air pollution, particularly to $PM_{2.5}$, PM_{10} and SO_2, appears to be associated with a higher prevalence and/or increased severity of LUTS, especially those related to voiding. Our study implies that long-term exposure to air pollutants can negatively affect the quality of life of men with LUTS and provides interesting insights into the prevention and management of LUTS. Considering the high global prevalence of LUTS among older men and the widespread nature of air pollution, this finding has significant implications for public health.

Methods

Study design and participants

Study participants were recruited from the health screening center of Seoul National University Hospital (SNUH) in South Korea from January 1, 2015 to December 31, 2019. They received regular health screenings and filled out surveys including self-reporting screening tools for LUTS, lifestyle, current medication, and past medical history. A total of 9,948 men underwent screening health checkups during this period, and 7,979 participants were finally included after excluding those who were aged < 30 years ($n = 412$), with prostate cancer history ($n = 109$), receiving medications for benign prostate hyperplasia ($n = 497$), exhibiting pyuria ($n = 32$), or having missing clinical data ($n = 919$) (Fig. 1). All methods were performed in compliance with the applicable guidelines and regulations.

Assessment of exposure to air pollution

To evaluate air pollution exposure, we applied hourly measurements of air pollutants obtained from about 300 nationwide air quality surveillance locations managed by the *Ministry of the Environment of Korea* (https://www.airkorea.or.kr). The observational data, collected during the 365 days preceding each participant's health check-up date, include particulate matter ≤ 2.5 μm in diameter ($PM_{2.5}$), particulate matter ≤ 10 μm in diameter

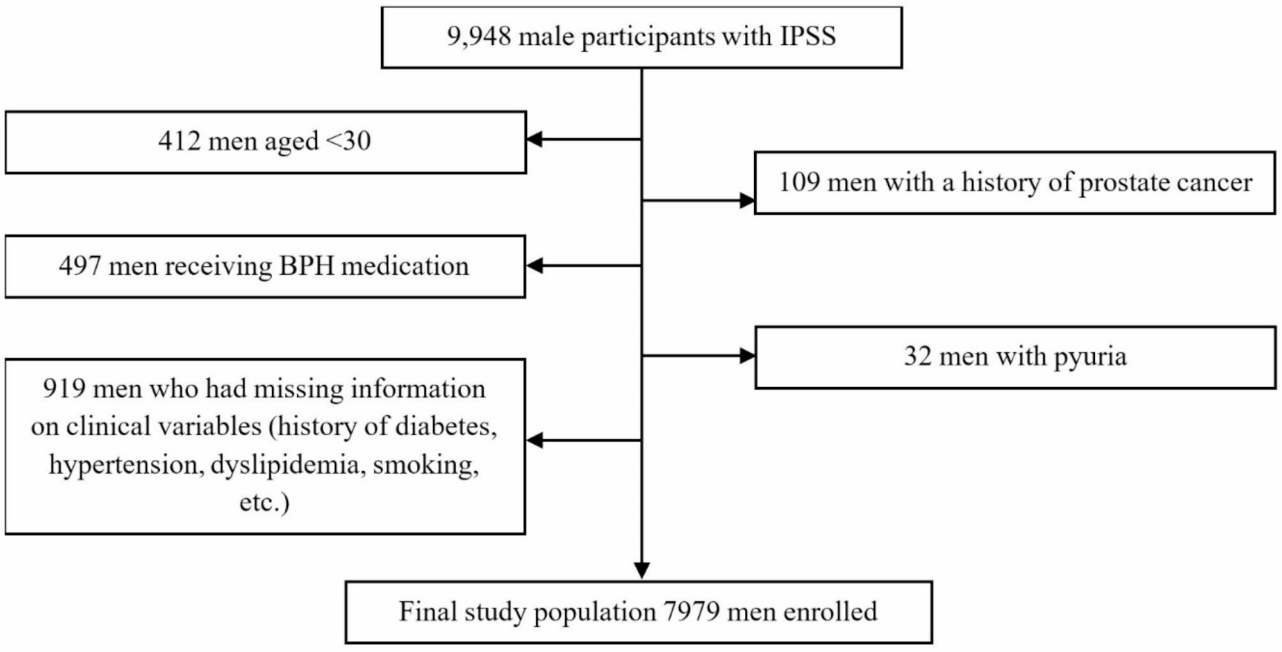

Fig. 1. Study flow diagram. *IPSS* international prostate symptom score, *BPH* benign prostate hyperplasia, *PSA* Prostate-specific antigen.

(PM_{10}), nitrogen dioxide (NO_2), sulfur dioxide (SO_2), carbon monoxide (CO), and ozone (O_3). For example, if a check-up was on March 5, 2018, air pollution exposure was averaged from March 5, 2017, to March 4, 2018. The modeling data, which were used to derive the annual mean exposure to air pollutants based on the participants' residential addresses at the time of their health check-ups, were used to subsidize the observational data. The modeling methods have been described in detail in several previous studies[24,25]. Briefly, we applied the Community Multiscale Air Quality (CMAQ, version 4.7.1) model developed by the *US Environmental Protection Agency* to simulate the ambient concentrations of primary and secondary air pollutants. Weather Research and Forecasting (WRF, version 3.9) and Sparse Matrix Operator Kern el Emissions (SMOKE, version 3.1) models were used to create the meteorological and emission data for the CMAQ. For the chemical transport modeling system, a modeling domain with a 9-km horizontal grid resolution (67 × 82 grids) was set up to cover South Korea. The observational data, with help from modeling data to compensate for missing data, were spatially interpolated to prepare air pollution data for the 250 administrative districts where the participants resided.

Assessment of LUTS

LUTS were assessed using the *International Prostate Symptom Score* (IPSS). The IPSS is a self-reported survey composing 7 questions scored from 0 (representing "not at all") to 5 (representing "almost always"). Based on the cumulative scores of each item, which may vary from 0 to 35, the overall symptom severity was classified as non-to-mild (from 0 to 7 points) or moderate-to-severe (from 8 to 35 points). According to previous studies, IPSS score of 8 or higher was defined as LUTS[26–35]. Symptoms were categorized into two distinct groups: (1) voiding (obstructive) issues, such as intermittency, weak stream, incomplete bladder emptying, and straining, and (2) storage (irritative) issues, such as urinary urgency, nocturia, and urinary frequency. Moderate to severe symptoms were defined as a score of 5 or more out of 20 voiding symptoms and 4 or more out of 15 storage symptoms. In addition to the presence or absence of LUTS, we considered IPSS values as outcome variables in our analysis to identify the correlation between air pollution exposure and the severity of LUTS.

Potential covariates

To adjust for potential confounding variables, we included demographic data such as age, body mass index (BMI), smoking status, alcohol consumption, comorbidity, and laboratory data containing prostate-specific antigen (PSA). BMI was calculated by dividing weight in kilograms by the square of height in meters. Smoking status was classified into three categories: "never smoked," "former smoker," or "current smoker." Daily alcohol consumption was calculated by multiplying the weekly frequency of drinks consumed by the standard drink size, then dividing the result by 7. Alcohol consumption was categorized as "non-drinking", "less than two", or "two or more drinks" per day. Hypertension was characterized by systolic blood pressure (BP) equal to or greater than 140 mmHg, diastolic BP equal to or greater than 90 mmHg, or the use of antihypertensive medication. Dyslipidemia was characterized by low-density lipoprotein-cholesterol equal to or greater than 130, or the use of lipid-lowering medication. Diabetes mellitus was characterized by fasting glucose equal to or greater than 126, HbA1c equal to or greater than 6.5, or the use of diabetes medication.

Statistical analysis

Baseline characteristics were presented as means and standard deviations (SDs) for continuous variables and as numbers (%) for categorical variables. Between-group differences were identified using a two-tailed Student's *t*-test for continuous variables and the chi-squared test for categorical variables. Pearson's correlation analysis was used to test the correlations among the annual concentrations of each air pollutant. To evaluate the associations between exposure to air pollutants and LUTS, logistic regression analysis was performed in crude and adjusted models. The adjusted models included age, hypertension, dyslipidemia, diabetes mellitus, BMI, smoking status, categorized daily alcohol consumption, serum PSA level, and O_3 as covariates. The association results for moderate to severe LUTS were indicated as odds ratios (ORs) and 95% confidence intervals (CIs) for each air pollutant. We also performed linear regression analysis to evaluate the association between air pollution exposure and the severity level of LUTS in crude and adjusted models. The results for the severity level of LUTS were presented as beta coefficients (βs) and 95% CIs for each air pollutant. The estimates from the logistic and linear regression models were converted to interquartile range (IQR) for each pollutant. Furthermore, we conducted association analyses according to the symptoms of LUTS, such as voiding and storage. All analyses were performed using STATA version 18.1.

Data availability

The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

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Author contributions

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Declarations

Competing interests

The authors declare no competing interests.

Ethics statement

All research procedures were performed in accordance with relevant guidelines and regulations, including the Declaration of Helsinki as a statement of ethical principles for medical research involving human participants. The study protocol was reviewed and approved by the Seoul National University Hospital Institutional Review Board (IRB No. H-2307-168-1453). Due to the retrospective nature of the study, the need of obtaining informed consent was waived by the Seoul National University Hospital Institutional Review Board.

Additional information

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