Effects of Air Pollutants on Mortality of Chronic Kidney Disease Patients with Green Spaces Exposure: A Large Observational Study

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Abstract

With increasing air pollution, the association between green space exposure and health outcomes is a global health concern. The relationship between air pollution and the survival of patients with chronic kidney disease (CKD) who are exposed to residential greenness is yet to be elucidated. This study aimed to determine this relationship in Seoul between 2002 and 2015.

A time-varying survival analysis was conducted to investigate the association between long-term exposure to air pollutants and mortality in 29,602 patients with CKD living in residential environments with small and large green infrastructure. The low and high index groups were defined using continuous and percentile thresholds of the satellite data—the derived average Normalized Difference Vegetation Index within 250 m and 1,250 m of residence, respectively.

During the observation, 3,863 (14%) deaths occurred. The effect of air pollution exposure on mortality was worse in the low index group than in the high index group. Particularly, exposure to SO₂ was associated with increased mortality risk, regardless of the greenness threshold. Consistent results were observed in co-pollutant models. High greenery exposure significantly reduced the risk of air pollution related mortality. Our results emphasize the need for creating environmental infrastructures that include green spaces.

Introduction

Chronic kidney disease (CKD), which is indicated by a glomerular filtration rate less than 60 mL/min/1.73 m² for more than 3 months, is a condition in which the kidney function or structure becomes weakened^[1] and is recognized as a major public health problem worldwide. The prevalence rates of CKD in Norway and the United States were estimated as 10.2% and 11.0% in the 1990s, respectively, in a large population cohort study^[2]. Unlike traditional risk factors such as glomerulonephritis, hypertension, and diabetes mellitus^[3], environmental exposure to pollutants has increasingly become a cause of kidney disease. Moreover, the kidney is susceptible to air pollution because of its filtration function^[4]. A study conducted on a cohort of US veterans found that long-term exposure to particulate matter less than 10 µm [PM₁₀], nitrogen dioxide [NO₂], and carbon monoxide [CO], increased the risk of CKD incidence by 7%, 9%, and 10%, respectively^[5]. In addition, research conducted in Korea between 2007 and 2011 showed that increases in annual mean concentrations of PM₁₀ and NO₂ were associated with a decrease in the estimated glomerular filtration rate (eGFR) by 46% and 15%, respectively^[6]. As shown in the above-mentioned research, exposure to ambient air pollution has been one of the major risk factors for the loss of kidney function.

Considering the threat of air pollutant exposure to humanity, adaptation of green infrastructure is emerging as a solution; generally, this is directly related to the ability to reduce extreme heat and precipitation^[7]. Furthermore, it is widely understood that exposure to greenery has positive effects on

health by moderating ground temperature^[8], filtering pollutants from the air^[9], improving cardiovascular and mental health issues^[10], and providing space for exercise and social interaction^[11]. In particular, previous studies have investigated the preventive role of exposure to green spaces on the adverse health effects of ambient air pollution. A study conducted in Barcelona from 2008 to 2009 found that 54 pregnant women with residential exposure to green spaces were exposed to lower levels of outdoor PM_{2.5}^[12]. Another study with a cohort of 12,873 participants showed that the hazard ratio (HR) of all-cause mortality was 1.07 (1.02–1.11) in the highest tertile of the Normalized Difference Vegetation Index (NDVI; 0.53–0.96), with a 10 µg/m³ increase in the 3-year average PM_{2.5} concentration, compared with 1.10 (1.06–1.14) in the lowest NDVI (-0.14 to 0.30)^[13]. However, to the best of our knowledge, only few studies have reported the association between exposure to air pollution and mortality from CKD based on patients' exposure to green spaces.

In this study, we aimed to examine the association between exposure to ambient air pollutants and the risk of mortality in CKD patients with high and low greenness exposures, using a large observational cohort in Seoul, Korea.

Methods

Ethical aspects

The study complied with the Declaration of Helsinki and the Declaration of Istanbul and received full approval from the Institutional Review Boards of Seoul National University Hospital (approval number: J-1704-121-848), Seoul National University Bundang Hospital (approval number: B-1706/401-402), and Seoul National University Boramae Medical Center (approval number: 20170414/16-2017-65/051).

Study population and covariates

The retrospective cohort consisted of 32,949 participants diagnosed with CKD in three medical centers (Seoul National University Hospital, Seoul National University Bundang Hospital, and Seoul National University Boramae Medical Center) between January 2000 and December 2015. We excluded patients with less than three months of cohort participation (n = 7) for the diagnosis of CKD.

We collected data on 32,949 participants since 2000; however, the number of participants was limited because, although air pollutant data except that for particulate matter less than 2.5 µm [PM_{2.5}] was available since 2001, PM_{2.5} data was only measured from 2007. Therefore, 29,602 patients were included in the analyses of PM₁₀, NO₂, sulfur dioxide [SO₂], CO, and ozone [O₃] between January 2002 and December 2015, while the effects of PM_{2.5} on mortality were estimated in 18,717 participants between January 2008 and December 2015.

We obtained demographic and medical data on the participants retrospectively such as coordinates of their residence, sex, age, and eGFR, which indicated kidney function, hemoglobin, and categories of

diagnoses of diabetes and hypertension (0: not diagnosed, 1: presence), at enrolment. The mortality date was confirmed from Statistics Korea. Additionally, we assigned area-level characteristics obtained from Statistics Korea, such as the population density, the number of hospital beds, and the rate of financial independence, to each participant, based on the district of the residential address of each participant in the enrollment year.

Air pollution data

Hourly air pollution data ($PM_{2.5}$, PM_{10} , NO_2 , SO_2 , CO , and O_3) were obtained from the monitoring stations in 25 districts in Seoul. A district is the basic local government unit that provides administrative services in Seoul, and it ranges in area from 10 km² to 47 km². Data were obtained from the Korean National Institute of Environmental Research and Seoul Research Institute of Public Health and Environment between 2001 and 2015. We constructed daily average concentrations of $PM_{2.5}$ and PM_{10} in $\mu g/m^3$, NO_2 and SO_2 in parts per billion (ppb), and CO in parts per million (ppm) and the daily maximum 8-hour average O_3 concentration in ppb. To construct time-varying exposure to air pollutants, we calculated the annual average concentration of each air pollutant ($PM_{2.5}$, PM_{10} , NO_2 , SO_2 , CO) from 1 year before cohort enrollment to the date of censored status in each participant's residential district. Owing to the strong seasonality of O_3 concentrations, its annual average concentration during the summer months was assigned to the participants.

Normalized Difference Vegetation Index

The NDVI has been used as a representative indicator of greenness exposure in previous epidemiological studies^[14, 15]. NASA's Earth Observing System provided the NDVI obtained from the Terra Moderate Resolution Imaging Spectroradiometer (MODIS) Vegetation Indices (MOD13Q1) Version 6, which is generated every 16 days at a 250 m spatial resolution^[16]. The NDVI is calculated using visible (red) and near infrared (NIR) light, based on the characteristic that plants reflect most of the NIR light and not much visible red light $[(NIR-red)/(NIR+red)]$. Therefore, the NDVI ranges from -1 to 1, with -1 indicating water, and 1 indicating a dense green environment. We assigned the average exposure to residential greenness for each participant's geocoded residence within 250 m and 1,250 m radii during the summer months (June–August), 1 year before cohort enrolment, because the NDVI experiences seasonality. The average greenness value within 250 m and 1,250 m radii of the participant's residence indicated a measurement of the greenness directly accessible outside each home and the greenness within a 10–15 minute walk of the home, respectively.

Statistical analysis

To investigate the long-term effects of air pollutants ($PM_{2.5}$, PM_{10} , NO_2 , SO_2 , CO , and O_3) on the mortality of CKD patients, while considering the stratified effects of greenness, a time-dependent Cox model was used. The annual NDVI exposures for each participant during the summer months were classified into higher and lower green areas using continuous and categorical NDVI criteria. Using these greenery distributions, the NDVI standards were divided based on continuous values of 0.3, 0.35, and 0.4, and

percentiles of 50%, 75%, and 90%. The Hazard Ratios (HRs) and 95% confidence intervals (CIs) were estimated in fully adjusted models stratified by sex and 5-year age groups and adjusted by eGFR at baseline, hemoglobin, diabetes, hypertension, population density, number of hospital beds, and financial independence rate. Unlike the NDVI exposure, we reflected the time-varying characteristics of air pollution from 1 year before enrollment to the censoring date. In addition, we calculated survival time from the date of cohort entry to the censoring date, censoring patients at the date of death or end date of follow-up (December 31, 2015). We constructed co-pollutant models based on the correlation among pollutants to confirm their robustness. The results are presented as HRs with interquartile range (IQR) increase, which is the difference between the 75th and 25th percentiles of air pollutant concentration. All statistical analyses were conducted using R version 3.6.1 (Foundation for Statistical Computing, Vienna, Austria).

Results

Table 1 shows the baseline characteristics of the 29,602 CKD patients in Seoul, Korea. The NDVI exposure around the 1,250 m buffer, which was within walking distance, was higher overall, compared to the 250 m buffer. The average was calculated to be 0.31 at 250 m (dotted) and 0.33 at 1,250 m (two-dashed) radii (Figure. 1). When patients were divided according to a 50% concentration of the 250 m buffer, people living in areas with more greenness had less deaths, older age, and lower population density than participants in the area with less greenness. We found no differences in sex, eGFR, or diabetes diagnosis between the two groups. When classifying the NDVI group by percentile and continuous threshold, the group differences of air pollutant concentration between low and high NDVI spaces were all significant (Table S1). The average exposure concentrations of air pollutants in the high NDVI areas were lower than those in the low NDVI areas, except for O₃.

Table 1. Baseline characteristics of participants in low and high-NDVI groups

Abbreviation: NDVI, Normalized Difference Vegetation Index

We calculated HRs and 95% CIs associated with the IQR increase in air pollutant concentrations, by considering the interaction with green space as classified by various criteria. When the green area was classified by 75% of the NDVI exposure around the 250 m buffer, the HRs (95% CI) per IQR increase in the concentrations of PM_{2.5}, PM₁₀, NO₂, SO₂, CO, and O₃ in the high NDVI area were 1.00 (0.74–1.34), 0.80 (0.56–1.16), 1.01 (0.82–1.24), 0.93 (0.76–1.14), 1.03 (0.86–1.23), and 1.00 (0.79–1.26), respectively. These compared with 1.06 (0.90–1.24), 1.15 (0.98–1.34), 1.12 (1.01–1.24), 1.14 (1.03–1.25), 1.08 (0.99–1.17), and 1.09 (0.96–1.25) in the low NDVI area (Figure. 2 and Table S2). Consistent results using the 1,250 m buffer were shown for PM_{2.5} (1.06 [0.90–1.25] for the low group and 1.00 [0.74–1.35] for the high group), PM₁₀ (1.12 [0.96–1.32] for the low group and 0.88 [0.58–1.32] for the high group), SO₂ (1.12 [1.01–1.23] for low and 1.00 [0.81–1.23] for high), CO (1.08 [0.99–1.17] for low and 0.98 [0.81–1.19] for high), and O₃ (1.15 [1.01–1.32] for low and 0.92 [0.73–1.16] for high). Although there were differences in pollutant concentrations, the mortality risk associated with air pollution in CKD patients with high exposure to greenery was lower than that in those with low greenery exposure. In addition, the HRs

Variable	Total	Low NDVI	High NDVI	p-value
The number of participants	29,602	14,801	14,801	
Death counts	3,863 (13%)	2,136	1,727	< 0.001
Sex				
Male	14,181 (47%)	7,065	7,111	0.6
Female	15,427 (53%)	7,736	7,690	
Age	55.31 ± 17.02	54.79 ± 16.89	55.84 ± 17.14	< 0.001
eGFR	64.39 ± 29.22	64.44 ± 28.60	64.38 ± 29.89	0.9
Hemoglobin	13.00 ± 2.16	13.04 ± 2.16	12.96 ± 2.15	0.004
Diabetes				
Yes	6,219 (21%)	3,144	3,075	0.3
No	23,383 (79%)	11,657	11,726	
Hypertension				
Yes	9,726 (33%)	4,765	4,961	0.004
No	19,876 (67%)	10,036	9,840	
Population density (person/km ²)	17,757 ± 5,213	17,985 ± 5,498	17,564 ± 4,869	< 0.001
Number of hospital beds	2,669 ± 1,343	2,707 ± 1,450	2,632 ± 1,225	< 0.001
Financial independence rate (%)	44.38 ± 18.20	46.51 ± 17.95	41.15 ± 17.40	< 0.001

decreased in patients with high greenery exposure, compared to those with low greenery exposure. Consistent results were found in the high-NDVI environment classified by continuous criteria (Figure. 3 and Table S3).

Co-pollutant models were used to confirm the robustness of the main analyses. Before implementing the two-pollutant models, we calculated the correlation between the air pollutants (Figure S1). When the correlation coefficient was 0.7 or more, we excluded the variable from the co-pollutant model because of collinearity. For example, when analyzing the effect of PM_{2.5} on the mortality of CKD patients, PM₁₀ was excluded from the two-pollutant model because the correlation with PM₁₀ was large at 0.88. Therefore, the effects of PM_{2.5}, associated with mortality risk were analyzed in a single model and in a two-pollutant model with NO₂ and SO₂, respectively. Robust results were shown in the co-pollutant model (Figures S2–S7). HRs tended to increase in high NDVI areas by some greenery standards and buffers. However, the IQR increase in the concentration of each air pollutant had an increased effect on mortality in low NDVI areas than in high NDVI areas, and its significance disappeared, generally. For example, when using the

NDVI threshold within the 250 m buffer by 0.35, HRs in the low NDVI group were 1.18 (1.00–1.38) for PM₁₀ only, 1.16 (0.98–1.37) for PM₁₀ with NO₂, 1.19 (1.01–1.40) for PM₁₀ with SO₂, and 1.17 (1.00–1.38) for PM₁₀ with CO; whereas 0.78 (0.55–1.09), 0.74 (0.53–1.05), 0.77 (0.55–1.08), and 0.76 (0.54–1.08), were found for the high NDVI group, respectively. The protective effects of greenery exposure against air pollution were greater when exposed at a 250 m radius rather than a 1,250 m radius.

Discussion

This study explored the association between long-term exposure to air pollution and the mortality risk of approximately 30,000 CKD patients exposed to high and low levels of vegetation in Seoul, Korea. The risk effects of air pollution associated with mortality in low NDVI areas were greater than those in high NDVI areas, indicating that green environment could reduce the mortality risk associated with air pollution. Our findings are consistent with the results observed in co-pollutant models.

An approximately 10-year study found an association between mortality from respiratory diseases in 66,820 elderly individuals aged 65 years or older, and air pollutants (PM_{2.5}, PM₁₀, NO₂, and O₃) in areas with low and high greenness, using a time-stratified case-crossover design^[17]. The percent excess risk and 95% CI per 10 µg/m³ increase in a 4-day moving average of PM_{2.5}, NO₂, and O₃ for pneumonia were -3.57 (-9.06 to 1.95), -3.22 (-9.15 to 2.75), and -5.20 (-10.68 to 0.31) in the high NDVI areas, compared to 3.25 (-2.25 to 8.79), 4.58 (-1.23 to 10.41), and 3.12 (-2.31 to 8.59) in the low NDVI areas, respectively. In a Korean study examining the health effects of PM₁₀ on green areas, percent changes in non-accidental mortality per 10 µg/m³ increase of PM₁₀ were 5.83% (3.95–7.74%) and 3.45% (1.42–5.51%) in high-level and low-level green areas, respectively^[18]. Although a higher risk of non-accidental disease was shown in greener spaces, cardiovascular mortality rate was estimated to increase by 7.46% (3.97–11.07%) in the high-green area and 11.23% (7.28–15.32%) in the low-green area. Likewise, studies examining the health effects associated with air pollution and residential greenness were in the implementation stage, and findings regarding the protective effects of greenery exposure were inconsistent

Two representative theories could explain our results showing that the effects of air pollution could be reduced using green infrastructure^[19]. First, urban vegetation typically removes a few percent of air pollutants by depositing them onto the leaves. However, this effect is not often apparent in urban areas and is usually seen in forested areas. Dispersion, however, is more important than deposition for reducing air pollution exposure in downtown areas. Air pollutants can be dispersed and diluted because green environment can control the speed, direction, and dispersion distance of air pollutants^[20]. In other words, exposure to green spaces can play a role in maintaining the distribution of air pollutants, and reduced air pollution may be associated with decreased mortality risk in areas with more residential greenness. The underlying mechanisms of the effects of air pollution associated with greenness in patients with CKD are unknown. However, this may be because the health benefits of green space exposure are related to various pathways; these benefits include reducing air pollution and noise and enabling stress alleviation and relaxation^[21].

Our study compared the average exposure rate to air pollutants between patients living in areas with low and high levels of green infrastructure. Reduced concentrations of air pollutants in high vegetation areas were observed, except for O₃. A previous study conducted in Spain supported the contribution of urban forests regulating services to the mitigation of pollution (305.6 tons [t] of removed air pollutants and 19036 t of CO₂ equivalent per year)^[22]. In addition, a study conducted in the United States showed that one of the ways that urban trees affect air quality is pollution removal, showing an estimated total removal of 711,000 metric tons (\$3.8 billion value) of pollutants (O₃, PM₁₀, NO₂, SO₂, and CO)^[23]. However, the results of research on the reduction effect of O₃ on greenery exposure are controversial. Previous studies have reported that certain tree types can emit isoprene in areas with enough pollutants during periods of extensive heat and weak winds, which increases the concentration of O₃ in the atmosphere^[24]. Furthermore, yearly O₃ removal differed according to tree functional groups (evergreen broadleaves, deciduous broadleaves, conifers, and actual functional groups), classified by tree cover, leaf season length, and physiology^[25]. Therefore, O₃ concentration depends on vegetation characteristics, such as tree species, physiological status, and surrounding environment, such as climate and distribution of atmospheric chemicals^[26]. Although O₃ concentration was high in green areas, the effects of health risk associated with air pollutants in high vegetation areas were lower than in the low vegetation areas. There were no clear explanations for these associations. However, the health effects may differ depending on the O₃ source (emissions from leaves in plants or created by chemical reactions between oxides of nitrogen [NO_x] and volatile organic compounds [VOCs] from cars and industrial sources). Another reason why the risk size of ambient O₃ concentration on health was smaller is due to the complex effect of greenery exposure on human health.

Our study showed distinct risk effects of SO₂ associated with the mortality of CKD patients living in low vegetation areas, regardless of the buffer and criteria of residential NDVI. SO₂ emitted from fossil fuel combustion by both industrial processes and power plants induces stomatal closure at high concentrations, resulting in photosynthesis reduction and general water stress in leaves^[27]. These mechanisms protect plants from rapid detoxification to avoid injury. Therefore, visible symptoms such as abscission of older leaves and tip necrosis in flowers were commonly observed due to SO₂ pollution^[28]. Weakened plant functions may interfere with the pathways of residential greenness, affecting health at high SO₂ concentrations in low vegetation areas.

Our study has some limitations. First, the results from epidemiologic studies may contain exposure measurement errors for actual exposure and ambient air pollution. Second, we could not adjust for potential confounders, such as physical activity and lifestyle, because of lack of data availability. Finally, our data could not explain the underlying mechanism of the negative health effects associated with O₃ in low greenery areas, despite low concentrations. However, we observed protective effects of vegetations related to air pollutants in a large observational cohort in a metropolitan city.

Conclusions

In conclusion, green infrastructure could reduce the concentrations of air pollutants, except O₃, and provide positive health benefits to CKD patients through various pathways. Therefore, it is necessary to create a planned and phased green environment.

Abbreviations

Confidence interval, CI; Chronic kidney disease, CKD; carbon monoxide, CO; hazard ratio, HR; interquartile range, IQR; Normalized Difference Vegetation Index, NDVI; particulate matter less than 2.5 µm, PM_{2.5}; particulate matter less than 10.0 µm, PM₁₀.

Declarations

Acknowledgments

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Authors' contributions

JJ and HK participated in conceptualization. YCK, JPL, and SK contributed in data curation. JJ and HL participated in analysis. SJS, YSK, and SK advised the interpretation. JYP and HK supervised the project. All authors reviewed and approved the final version of the manuscript.

Ethics approval and consent to participate

The study complied with the Declaration of Helsinki and the Declaration of Istanbul. The cohort is based on retrospective data which is unavailable to obtain individual consents, and therefore we proceeded with the exemption of consent as follows; full approval from the Institutional Review Boards of Seoul National University Hospital (approval number: J-1704-121-848), Seoul National University Bundang Hospital (approval number: B-1706/401-402), and Seoul National University Boramae Medical Center (approval number: 20170414/16-2017-65/051).

Consent for publication

Not applicable

Availability of data and material

The datasets are available after coauthors' approval.

Competing interests

The authors declare no conflict of interest.

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Figures

Figure 1

NDVI exposure distribution of 29 602 CKD patients in Seoul, Korea

Figure 2

Association between IQR increase in air pollution and risk of mortality by percentile

Figure 3

Association between IQR increase in air pollution and risk of mortality by continuous value

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