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# The renal adverse effect of PM 2.5 and NO2 after adjusting medication usage in diabetic kidney disease patients

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**Objectives:** There is increasing evidence that air pollutants adversely affect renal function in chronic kidney disease. Also, exposure to air pollution increases the incidence of type 2 diabetes and insulin resistance. Although, the evaluation of the air pollution effect in diabetic kidney disease (DKD) patients is insufficient. Moreover, the effect of medications that mainly affect the prognosis was not properly accessed. We investigated the effect of air pollutants in DKD patients with detailed adjustment of medication usage.

**Methods:** This retrospective cohort study enrolled DKD patients from two South Korean tertiary-referral centers. A primary outcome was an incident event of end-stage kidney disease (ESKD). We collected national-wide monthly information on four air pollutants (PM2.5, PM10, NO2, and CO) from 2000 to 2020. Prescription information of oral anti-diabetic drugs (metformin, sulfonylurea [SU], and DPP-4 inhibitors), insulin, and renin-angiotensin system inhibitor were collected from each hospital. A multivariable time-dependent Cox analysis was conducted, and the air pollutants and medication usage were considered as time-varying variables.

**Results:** Among 10,010 patients, a total of 1,884 patients (18.8%) progressed to ESRD during a median follow-up period of 98 months [interquartile range, 48; 157]. During the follow-up, the prescription ratio of metformin and DPP-4 inhibitors increased continuously. Whereas, the proportion of SU and insulin were constants over time (Figure 1). In univariate analysis, the increment of PM 2.5 was associated with an increased risk of incident ESKD (hazard ratio [HR] 1.04, 95% confidence interval [CI] 1.019—1.052). After adjustment of baseline characteristics and time-varying medication usage, the increased PM 2.5 (adjusted HR [aHR] 1.02, 95% CI 1.009—1.041) and NO2 (aHR 1.02, 95% CI 1.004—1.028, Table 1) concentration were associated with increased risk of ESKD.

**Conclusions:** In the present study, there was evidence of adverse effects related to exposure to PM2.5 and NO2 in ESKD progression even after comprehensive adjustment of medication.

The medication prescription proportion of present cohort

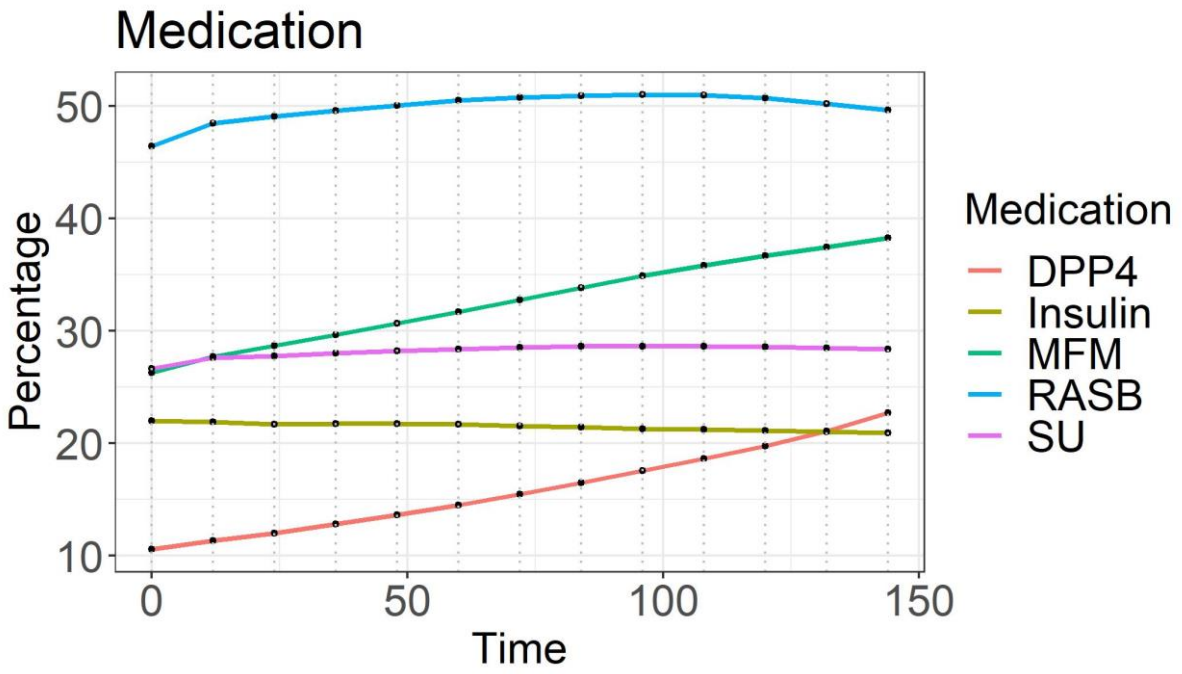


Table 1. Risk of incident ESKD for each air pollutants considering time-varying concentration over time.

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| | Univariate | | Multivariable[#] | |
|---|---|---|---|---|
| | HR | 95% CI | HR | 95% CI |
| NO2 | 1.00 | 0.989—1.011 | 1.02 | 1.004—1.028 |
| CO | 1.00 | 0.998—1.001 | 1.00 | 0.998—1.000 |
| PM10 | 0.99 | 0.982—0.993 | 0.99 | 0.987—0.998 |
| PM2.5 | 1.04 | 1.019—1.052 | 1.02 | 1.009—1.041 |

[#] adjusted for time fixed baseline characteristics (age, sex, hospital, body mass index, smoking, hypertension, coronary artery disease, and dyslipidemia and initial laboratory findings [estimated glomerular filtration rate, hemoglbinA1c, and albumin]) and time-varying medication usage (metformin, sulfonylurea, DPP-4 inhibitor, insulin and RAS blocker)