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Traffic-related air pollution associated with chronic kidney disease among elderly residents in Taipei City☆

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ABSTRACT

The associations of air pollution with chronic kidney disease (CKD) have not yet been fully studied. We enrolled 8,497 Taipei City residents older than 65 years and calculated the estimated glomerular filtration rate (eGFR) using the Taiwanese Chronic Kidney Disease Epidemiology Collaboration equation. Proteinuria was assessed via dipstick on voided urine. CKD prevalence and risk of progression were defined according to the KDIGO 2012 guidelines. Land-use regression models were used to estimate the participants' one-year exposures to PM of different sizes and traffic-related exhaust, $PM_{2.5}$ absorbance, nitrogen dioxide (NO_2), and NO_x. Generalized linear regressions and logistic regressions were used to examine the associations of one-year air pollution exposures with eGFR, proteinuria, CKD prevalence and risk of progression. The results showed that the interquartile range (IQR) increments of $PM_{2.5}$ absorbance (0.4×10^{-5}/m) and NO_2 (7.0 μg/m^3) were associated with a 1.07% [95% confidence interval (CI): 0.54−1.57] and 0.84% (95% CI: 0.37−1.32) lower eGFR, respectively; such relationships were magnified in subjects who had an eGFR >60 ml/min/1.73 m^2 or who were non-diabetic. Similar associations were also observed for PM_{10} and $PM_{2.5-10}$. Two-pollutant models showed that PM_{10} and $PM_{2.5}$ absorbance were associated with a lower eGFR. The odd ratios (ORs) of CKD prevalence and risk of progression also increased with exposures to $PM_{2.5}$ absorbance and NO_2. In summary, one-year exposures to traffic-related air pollution were associated with lower eGFR, higher CKD prevalence, and increased risk of CKD progression among the elderly population. Air pollution-related impaired renal function was stronger in non-CKD and non-diabetic subjects.

1. Introduction

Chronic kidney disease (CKD) is a worldwide public health problem with a variety of adverse outcomes, including premature death, and it is regarded as a cardiovascular disease (CVD) risk equivalent (Go et al., 2004; Weiner et al., 2004). In addition to a dozen well-documented traditional risk factors, such as hypertension and diabetes, an increasing body of evidence demonstrates that air pollution may be a novel environmental risk factor of CKD. A sub-cohort study found that short-term particulate matter (PM) exposure was associated with increased urinary sodium excretion (Tsai et al., 2012). O'Neill et al. (2008) observed a weak acceleration in the progression of albuminuria during chronic exposure to ambient particles (PM_{10}). One hospital-based study also observed an association between long-term exposure to $PM_{2.5}$ and membrane nephropathy (Xu et al., 2016). Our previous study showed that PM of different sizes, including PM_{10} and coarse particles ($PM_{2.5-10}$), were associated with lower estimated glomerular filtration rate (eGFR) and higher CKD prevalence of general population in New Taipei City, Taiwan (Yang et al., 2017). A longitudinal study demonstrated the associations of $PM_{2.5}$ concentrations with higher risk of incident CKD and progression to end-stage renal disease (ESRD) (Bowe et al., 2017).

However, the vulnerability of renal dysfunction to the old age population and traffic-related air pollution are inconclusive. Mehta et al. (2016) demonstrated that one-year $PM_{2.5}$ exposure was associated with a lower eGFR among older men. Our previous study

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in New Taipei City contrarily reported PM_{10} and $PM_{2.5-10}$, but not $PM_{2.5}$, were associated with reduced eGFR and increased CKD prevalence, and the stratified analyses showed such relationships were only observed among subjects aged <65 years, but not in subjects aged ≥65 years (Yang et al., 2017). Prior studies also failed to demonstrate the different effects of emitted sources or pollutant compositions on renal function. Lue et al. (2013) found lower eGFR values in residents living near a major road, a coarse proxy of traffic indicator, that implies roadway exposures may contribute to impaired renal function; however, the relevance of traffic noise or socio-economic factors cannot be completely eliminated. The European Study of Cohorts for Air Pollution Effects (ESCAPE) project developed the land use regression (LUR) models to estimate one-year exposure to PM in different sizes and traffic-related air pollution, i.e. $PM_{2.5}$ absorbance, nitrogen dioxide (NO_2), and nitrogen oxides (NO_x) (Beelen et al., 2013; Eeftens et al., 2012a; Wang et al., 2013). Therefore, we applied a community-based elderly cohort in Taipei City, a neighboring city of New Taipei City in Yang et al. (2017), to examine the associations of eGFR, proteinuria, CKD prevalence, and the risk of CKD progression with one-year exposures to PM in different sizes and traffic-related air pollution among the elderly population.

2. Methods

2.1. Study population

We used a cross-sectional design in this study. The study subjects of Taipei City elderly cohort were selected from the Taipei City Elderly Health Screening Program in 2009. This program is an annual program run by the Taipei City Department of Health from March 1st to August 31st, 2009. All senior citizens over the age of 65 and residing in Taipei City are invited to participate in this health screening program every three years. There are two different packages provided by the health screening program, only one of which includes renal function examination and a urine dipstick test. All participants are allowed to choose one of these two packages for health examination according to their preference. The detailed information of this cohort has been described and published in another study (Chen et al., 2015). Overall, 42,105 senior citizens participated in this program in 2009. After excluding participants with missing information on adjustable variables or home addresses to estimate exposure, 27,752 participants were selected as candidates for this study. Participants who did not undergo the kidney function examination or urine protein analysis were also excluded, resulting in a total of 8,479 subjects who met the criteria for this study. The individual characteristics and exposed concentrations of air pollution were similar between the excluded and included subjects (Supplemental Table 1). A detailed flow chart from the health screening program displaying the recruitment process is shown in Fig. 1. The health dataset has been decoded, and personal information, including names and IDs, was unlinked from medical records. We obtained approval from the Taipei City Department of Health to use these data. This study was approved by the Joint Institutional Review Board of E-Da Hospital.

2.2. Health data

The health screening program was conducted in 10 branches of the Taipei Municipal Hospital and consisted of a clinician interview, a self-reported questionnaire, and venous blood biochemical analysis. The clinician interview record and questionnaire provided information including home address, age, sex, height, weight, body mass index (BMI), smoking status (current smoker vs. ex- or never-smoker), alcohol consumption (<1 drink/week, 1–3 drinks/week, or >3 drinks/week), physical activity (<1 h/week, 1–3 h/week, or >3 h/week), and education level (primary school or less, up to secondary school or equivalent, or university degree and above). Here, a standard drink of alcohol was defined as 0.6 fluid ounces or 14 g of pure alcohol, which is equal to 12 fluid ounces of beer, 5 fluid ounces of wine, or 1.5 fluid ounces of whisky. Physical activity was defined as planned, structured, or repetitive exercise. A fasting venous blood sample was collected to measure fasting blood glucose and lipid profile, including total cholesterol, triglycerides, high- and low-density lipoprotein cholesterol (HDL-C and LDL-C), and renal function (blood urea nitrogen and creatinine). In this study, subjects who either had self-reported physician-diagnosed hypertension and used anti-hypertensive medication or had measured blood pressure (BP) values ≥ 140 mmHg for systolic BP or ≥90 mmHg for diastolic BP were all defined as hypertensive subjects. Subjects who either had physician-diagnosed diabetes and used oral hypoglycemic agents or had measured fasting glucose ≥126 mg/dL were defined as diabetic subjects.

2.3. Outcome measurements

The eGFR and proteinuria were used as the outcome measures. The eGFR was based on age and serum creatinine (SC_r) level, which was measured by the isotope dilution mass spectrometry (IDMS)-traceable enzymatic method on an autoanalyzer (Toshiba 200FR, Tokyo, Japan). In this study, eGFR was calculated using the Taiwanese Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation, which was modified from the CKD-EPI equation and has been demonstrated to have a better diagnostic performance than CKD-EPI or Modification of Diet in Renal Disease (MDRD) equations for Taiwanese (Chen et al., 2014). The CKD-EPI-Taiwan equation equals 1.262 x $\text{CKD-EPI}^{0.914}$, whereas the CKD-EPI equation equals 141 x min $(SCr/\kappa, 1)^{\alpha}$ x max $(SCr/\kappa, 1)^{-1.209}$ x 0.993^{Age} x 1.018 [if female]; κ is 0.7 for females and 0.9 for males, α is −0.329 for females and −0.411 for males, min indicates the minimum of SCr/κ or 1, and max indicates the maximum of SCr/κ or 1 (Levey et al., 2003). CKD was defined as eGFR <60 ml/min/1.73 m^2 which represents a ≥50% reduction in normal kidney function (Levey et al., 2003). We also collected freshly voided urine samples and measured urine protein using the dipstick urine test (Roche Diagnostics K.K., Tokyo, Japan). The dipstick test for protein provides a semiquantitative estimation of protein concentration, with 5–20 mg/dL as trace, 30 mg/dL as 1+, 100 mg/dL as 2+, 300 mg/dL as 3+, and >1000 mg/dL as 4+. Proteinuria was defined as urine protein ≥1 + in the dipstick test. Lim et al. (2014) reported urine dipstick testing can be recommended for screening in older outpatients with 95.6% of sensitivity and 92.2% of specificity if albumin/creatinine ratio ≥300 mg/g was set as the reference standard for proteinuria. In order to examine the association between air pollution and the risk of CKD progression, we further categorized the risk of CKD progression of study subjects as very high-, high-, moderate-, or low-risk of CKD progression determined by GFR and urine protein dipstick values according to the guidelines from Kidney Disease: Improving Global Outcomes (KDIGO) 2012 (National Kidney Foundation, 2012). Here, low-risk of CKD progression was defined as eGFR ≥60 ml/min/1.73 m^2 and dipstick negative or trace; moderate-risk of CKD progression was defined as eGFR ≥60 ml/min/1.73 m^2 and dipstick 1 + or eGFR 45–59 ml/min/1.73 m^2 and dipstick negative or trace; high-risk of CKD progression was defined as eGFR 30–44 ml/min/1.73 m^2 and dipstick negative or trace, eGFR 45–59 ml/min/1.73 m^2 and dipstick 1+, or eGFR ≥60 ml/min/1.73 m^2 and dipstick ≥2+; and very high-risk of CKD progression was defined as eGFR <30 ml/min/1.73 m^2, eGFR 30–44 ml/min/1.73 m^2 and dipstick ≥1+, or eGFR 45–59 ml/min/1.73 m^2 and dipstick ≥2+.