Secondhand Smoke and Chronic Kidney Disease

Authors:

Jong Hyun Jhee, Young Su Joo, Youn Kyung Kee, Su-Young Jung, Seohyun Park, Chang-Yun Yoon, Seung Hyeok Han, Tae-Hyun Yoo, Shin-Wook Kang, and Jung Tak Park

Supplemental Material Table of Contents

Supplemental Table 1. The prevalence of CKD based on eGFR and proteinuria definition

Supplemental Table 2. Relative risk for the prevalence of CKD according to life-time total duration of secondhand smoke

Supplemental Table 3. Univariable associations between clinical factors and CKD in cross-sectional and prospective analysis

Supplemental Table 4. Relative risk for the prevalence of CKD according to ever smoker vs. never smoker

Supplemental Table 5. Relative risk for the prevalence of CKD according to frequency of secondhand smoke exposed at home and work

Supplemental Table 6. Baseline characteristics according to exposure location

Supplemental Table 7. Baseline characteristics according to two different cohort datasets

Supplemental Figure 1. Graphical evaluation of the proportional hazards assumption

Supplemental Figure 2. Causal diagram showing assumed associations between baseline secondhand smoke, chronic kidney disease, and baseline characteristics.

SUPPLEMENTAL METHODS

Anthropometric and laboratory data

All subjects received a comprehensive health examination, and filled out questionnaires on health and lifestyle at the time of study entry. Demographic and socioeconomic data, including age, sex, level of education and income, marital status, smoking status, alcohol intake, degree of physical activity, and medical histories were also collected. Anthropometric parameters such as height, body weight, and waist and hip circumferences were measured by skilled study workers following standard methods while the subjects were wearing light clothes. Body mass index (BMI) and waist-to-hip ratio were calculated as the weight divided by height squared (kg/m^2) and the waist circumference divided by the hip circumference, respectively. The level of education was divided into three groups: low, lower than middle school; middle, middle school; high, higher than middle school. The level of income was divided into three groups: low, <$850 per month; middle, $850 to $1,700 per month; high, ≥$1,700 per month. Physical activities were expressed as the metabolic equivalent of task. Subjects who had a history of hypertension, with a blood pressure of ≥140/90 mm Hg, or were taking antihypertensive agents were considered hypertensive. Those who had a medical history of diabetes, blood glucose levels ≥126 mg/dL in an 8-h fasting status, postload glucose levels ≥200 mg/dL after a 75-g oral glucose tolerance test, HbA1c ≥6.5%, or were receiving oral medication and/or insulin treatment for hyperglycemia were considered as having diabetes. Subjects with a medical history of dyslipidemia or taking medication for lipid control were considered as having dyslipidemia. Cardiovascular disease was defined as the composite of myocardial infarction, congestive heart failure, coronary artery disease, peripheral artery disease, and/or cerebrovascular accident.

The following biochemical data were determined by using fasting blood samples: concentrations of sodium, blood urea nitrogen, creatinine, hemoglobin, glucose, HbA1c, albumin, total cholesterol, triglyceride, high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), and C-reactive protein. LDL-C was calculated by using the Friedewald formula (1). Urine samples were collected in the morning after the first voiding. Fresh urine samples were analyzed by using URISCAN Pro II (YD Diagnostics Corp., Seoul, Korea).

Reference

1. Friedewald WT, Levy RI, Fredrickson DS: Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. *Clin Chem* 18(6): 499-502, 1972.

Supplemental Table 1. The prevalence of CKD based on eGFR and proteinuria definition*

	Case (%)	Model 1		Model 2		Model 3		Model 4	
		OR (96% CI)	*P*	OR (96% CI)	*P*	OR (96% CI)	*P*	OR (96% CI)	*P*
Secondhand smoke (yes vs. no)	358/16,694 (2)	1.23 (1.10-1.38)	<0.001	1.45 (1.27-1.66)	<0.001	1.37 (1.19-1.58)	<0.001	1.44 (1.26-1.65)	<0.001
Secondhand smoke frequency									
No-exposure	2,627/114,502 (2)	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)	
<3 days/week	80/3,710 (2)	1.34 (1.07-1.69)	0.01	1.74 (1.35-2.25)	<0.001	1.59 (1.21-2.10)	0.001	1.72 (1.33-2.22)	<0.001
≥3 days/week	278/12,984 (9)	1.20 (1.06-1.36)	0.01	1.37 (1.17-1.60)	<0.001	1.31 (1.11-1.54)	0.001	1.37 (1.17-1.60)	<0.001

Note: *CKD was defined as eGFR < 60 mL/min/1.73 m^2 or having higher than trace level proteinuria according to dipstick test results.

Model 1: Adjustment for age and sex

Model 2: Model 1 + demographic factors including BMI, systolic BP, history of hypertension, history of diabetes, alcohol status, education levels, income levels, and marital status

Model 3: Model 2 + laboratory factors including hemoglobin and serum albumin

Model 4: Adjustment for age, sex, history of hypertension, history of diabetes, alcohol status, education levels, income levels, and marital status

Abbreviations: CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; OR, odds ratio; CI, confidence; BMI, body mass index

Supplemental Table 2. Relative risk for the prevalence of CKD according to life-time total duration of secondhand smoke (n = 125,371)*

	Case (%)	Model 1		Model 2		Model 3		Model 4	
		OR (96% CI)	*P*	OR (96% CI)	*P*	OR (96% CI)	*P*	OR (96% CI)	*P*
Secondhand smoke exposure duration									
No-exposure	2,274/114,502 (2)	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)	
<10 years	40/3,018 (1)	1.09 (0.79-1.50)	0.61	1.22 (0.86-1.74)	0.26	1.09 (0.75-1.58)	0.66	1.19 (0.84-1.69)	0.34
10-19 years	42/3,022 (1)	1.43 (1.04-1.95)	0.03	1.46 (1.02-2.09)	0.04	1.28 (0.87-1.87)	0.21	1.47 (1.03-2.08)	0.03
≥20 years	144/4,829 (3)	1.52 (1.28-1.82)	<0.001	1.65 (1.34-2.03)	<0.001	1.62 (1.30-2.01)	<0.001	1.61 (1.31-2.00)	<0.001

Note: *Analysis was done in 125,371 subjects who had full information regarding life-time total secondhand smoke exposure duration.
Model 1: Adjustment for age and sex
Model 2: Model 1 + demographic factors including BMI, systolic BP, history of hypertension, history of diabetes, alcohol status, education levels, income levels, and marital status
Model 3: Model 2 + laboratory factors including hemoglobin and serum albumin
Model 4: Adjustment for age, sex, history of hypertension, history of diabetes, education levels, income levels, and marital status
Abbreviations: CKD, chronic kidney disease; OR, odds ratio; CI, confidence; BMI, body mass index; SBP, systolic blood pressure

Supplemental Table 3. Univariable associations between clinical factors and CKD in cross-sectional and prospective analysis

	Cross-sectional analysis		**Prospective analysis**	
	OR (95% CI)*	***P***	**HR (95% CI)†**	***P***
Age (per 1 year)	1.16 (1.15-1.17)	<0.001	1.12 (1.10-1.14)	<0.001
Sex (female vs. male)	1.60 (1.47-1.74)	<0.001	1.45 (1.01-2.08)	0.04
BMI (per 1 kg/m^2)	1.11 (1.10-1.13)	<0.001	1.08 (1.04-1.11)	<0.001
SBP (per 1 mmHg)	1.02 (1.01-1.03)	<0.001	1.02 (1.01-1.03)	<0.001
Alcohol status (yes vs. no)	0.80 (0.77-0.84)	<0.001	0.74 (0.65-0.84)	<0.001
Education levels				
≤Elementary	reference		reference	
Middle–high school	0.48 (0.44-0.53)	<0.001	0.44 (0.35-0.55)	<0.001
≥College	0.48 (0.43-0.53)	<0.001	0.42 (0.26-0.68)	<0.001
Income levels				
Low	reference		reference	
Intermediate	0.51 (0.46-0.57)	<0.001	0.52 (0.40-0.68)	<0.001
High	0.31 (0.27-0.34)	<0.001	0.48 (0.34-0.68)	<0.001
Marital status (yes vs. no)	0.57 (0.51-0.63)	<0.001	0.52 (0.36-0.74)	<0.001
Hypertension (yes vs. no)	4.91 (4.54-5.31)	<0.001	2.62 (1.82-3.77)	<0.001
Diabetes (yes vs. no)	4.34 (3.94-4.78)	<0.001	2.31 (1.78-2.99)	<0.001
Hemoglobin (per 1 g/dL)	0.89 (0.86-0.91)	<0.001	1.09 (1.01-1.18)	0.03
Albumin (per 1 g/dL)	0.72 (0.62-0.83)	<0.001	0.55 (0.37-0.81)	0.01
eGFR (per 1 mL/min/1.73m^2)	N/A		0.95 (0.94-0.96)	<0.001
Total cholesterol (per 1 mg/dL)	1.00 (0.99-1.01)	0.40	1.01 (1.00-1.02)	<0.001

Note: *Univariable logistic regression analysis was performed with CKD and each clinical factor.
†Univariable Cox analysis was performed for incident CKD and each clinical factor.
Abbreviations: BMI, body mass index; SBP, systolic blood pressure; eGFR, estimated glomerular filtration rate; N/A, not applicable

Supplemental Table 4. Relative risk for the prevalence of CKD according to ever smoker vs. never smoker (n* = 157,814)

	Case (%)	Model 1		Model 2		Model 3		Model 4	
		OR (96% CI)	*P*	OR (96% CI)	*P*	OR (96% CI)	*P*	OR (96% CI)	*P*
Smoking status									
Never smoker	2,575/131,196 (2)	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)	
Ever smoker	731/26,618 (3)	1.35 (1.23-1.49)	<0.001	1.35 (1.21-1.51)	<0.001	1.32 (1.18-1.48)	<0.001	1.37 (1.22-1.53)	<0.001

Note: *Non-smokers (131,196) plus current or ex-smokers who were initially excluded from the main analysis (26,618), Ever smokers include current and ex-smokers.

Model 1: Adjustment for age and sex

Model 2: Model 1 + demographic factors including BMI, systolic BP, history of hypertension, history of diabetes, alcohol status, education levels, income levels, and marital status

Model 3: Model 2 + laboratory factors including hemoglobin and serum albumin

Model 4: Adjustment for age, sex, history of hypertension, history of diabetes, education levels, income levels, and marital status

Abbreviations: CKD, chronic kidney disease; OR, odds ratio; CI, confidence; BMI, body mass index; SBP, systolic blood pressure

Supplemental Table 5. Relative risk for the prevalence of CKD according to frequency of secondhand smoke exposed at home and work

	At home		At work	
	OR (95% CI)	***P***	**OR (95% CI)**	***P***
Secondhand smoke frequency				
No-exposure	1.00 (reference)		1.00 (reference)	
<3 days/week	1.83 (1.18-2.84)	0.01	1.63 (1.11-2.40)	0.01
≥3 days/week	1.66 (1.35-2.04)	<0.001	1.02 (0.74-1.39)	0.38

Models were adjustment for age, sex, history of hypertension, history of diabetes, education levels, income levels, and marital status
Abbreviations: CKD, chronic kidney disease; OR, odds ratio; CI, confidence; BMI, body mass index; BP, blood pressure

Supplemental Table 6. Baseline characteristics according to exposure location

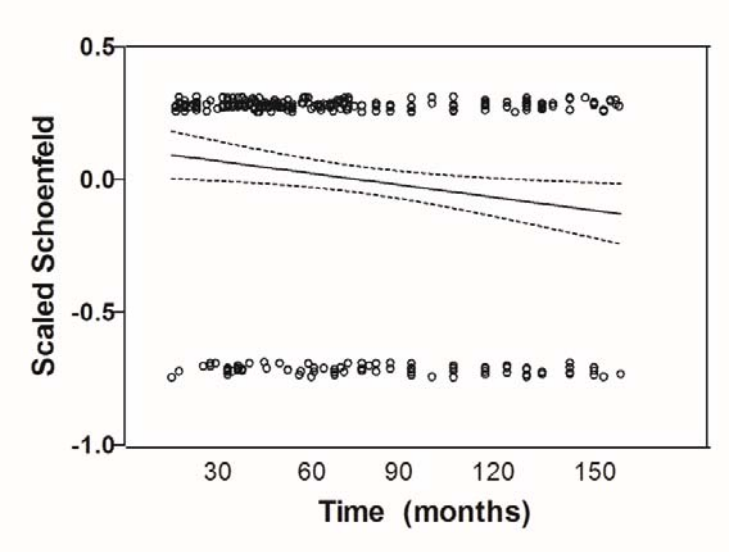
Characteristics	At home only (*n* = 10,020)	At work only (*n* = 4,011)
Secondhand smoke exposure		
Total duration (year)	24 ± 12	14 ± 12
Demographic data		
Age (years)	52 ± 8	50 ± 7
Female	9,819 (98.0)	2,428 (58.2)
BMI (kg/m^2)	24 ± 3	24 ± 3
Alcohol status (ever)	6,178 (62.0)	1,650 (39.7)
Physical activity (yes)	4,136 (49.2)	1,949 (51.9)
Married (yes)	7,584 (90.4)	3,149 (84.1)
Education status		
≤Elementary	3,380 (34.1)	801 (19.4)
Middle–high school	5,249 (52.9)	2,382 (57.6)
≥College	1,288 (13.0)	950 (23.0)
Income		
Low	1,636 (20.0)	340 (9.6)
Intermediate	3,714 (45.3)	1,594 (44.8)
High	2,846 (34.7)	1,625 (45.7)
Systolic BP (mm Hg)	121.5 ± 16.9	121.7 ± 15.6
Diastolic BP (mm Hg)	76.4 ± 10.5	77.3 ± 10.5
Comorbidities		
Hypertension	1,844 (18.4)	663 (15.9)
Diabetes	573 (5.7)	225 (5.4)
Dyslipidemia	655 (7.8)	247 (6.6)
Cardiovascular events	94 (1.1)	37 (1.0)
Laboratory data		
eGFR (mL/min/1.73 m^2)	90.1 ± 14.4	90.0 ± 13.9
Hemoglobin (g/dL)	13.0 ± 1.2	13.8 ± 1.5
Albumin (g/dL)	4.6 ± 0.3	4.7 ± 0.3
Glucose (mg/dL)	94 ± 23	94 ± 19
HbA1c (%)	5.7 ± 0.9	5.7 ± 0.9
Total cholesterol (mg/dL)	199 ± 36	195 ± 35
Triglyceride (mg/dL)	120 ± 80	120 ± 82
HDL-C (mg/dL)	55 ± 12	54 ± 13
LDL-C (mg/dL)	120 ± 32	117 ± 31
hs-CRP (mg/dL)	0.1 [0.0-0.2]	0.1 [0.0-0.1]

Note: Data are presented as mean ± standard deviation, median [interquartile range], or number (%).
Abbreviations: BMI, body mass index; eGFR, estimated glomerular filtration rate; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; hs-CRP, high-sensitivity C-reactive protein

Supplemental Table 7. Baseline characteristics according to two different cohort datasets

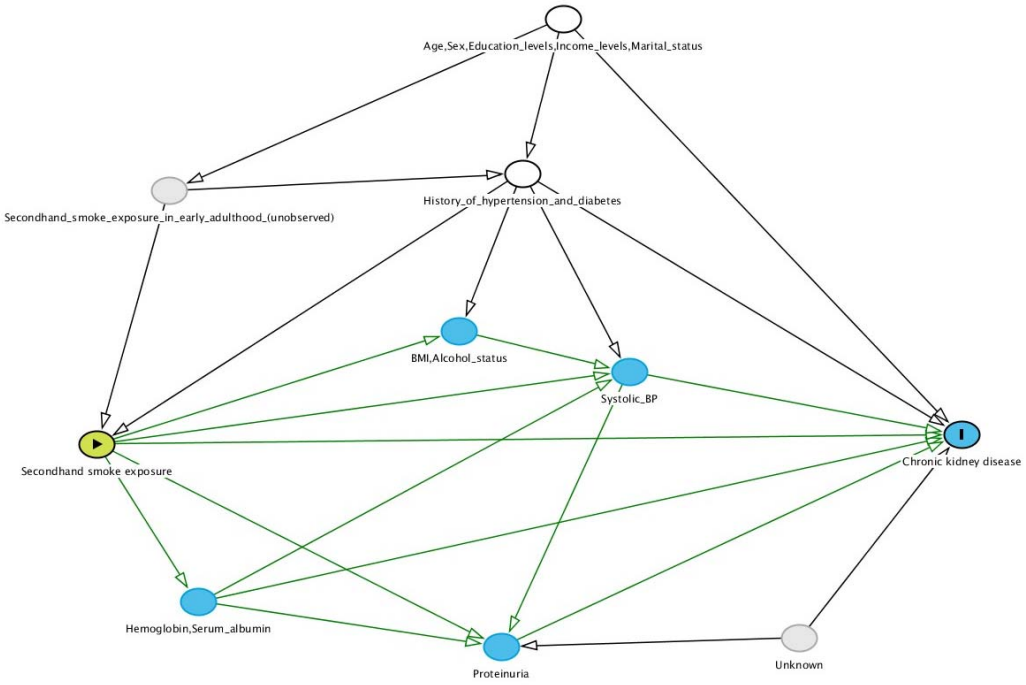
Characteristics	KoGES_HEXA study (*n* = 128,912)	KoGES_Ansan-Anseong study (*n* = 1,948)
Demographic data		
Age (years)	54 ± 8	52 ± 9
Female	99,262 (77)	1,626 (84)
BMI (kg/m^2)	24 ± 3	25 ± 3
Alcohol status (ever)	51,564 (40)	662 (34)
Physical activity (yes)	67,034 (52)	1,363 (70)
Married (yes)	109,575 (85)	1,714 (88)
Education status		
≤Elementary	24,493 (19)	1,227 (63)
Middle–high school	70,901 (55)	681 (35)
≥College	33,517 (26)	38 (2)
Income		
Low	14,180 (11)	720 (37)
Intermediate	46,408 (36)	896 (46)
High	48,986 (38)	292 (15)
Systolic BP (mm Hg)	122 ± 16	121 ± 19
Diastolic BP (mm Hg)	76 ± 10	80 ± 12
Comorbidities		
Hypertension	25,782 (20)	311 (16)
Diabetes	7,734 (6)	117 (6)
Dyslipidemia	11,602 (9)	37 (2)
Cardiovascular events	1,289 (1)	19 (1)
Laboratory data		
eGFR (mL/min/1.73 m^2)	91 ± 14	95 ± 14
Hemoglobin (g/dL)	13.6 ± 1.4	12.8 ± 1.4
Albumin (g/dL)	4.6 ± 0.3	4.5 ± 0.3
Glucose (mg/dL)	94 ± 21	91 ± 21
HbA1c (%)	5.7 ± 0.8	5.7 ± 0.7)
Total cholesterol (mg/dL)	198 ± 36	198 ± 36
Triglyceride (mg/dL)	121 ± 83	139 ± 98
HDL-C (mg/dL)	55 ± 13	51 ± 12
LDL-C (mg/dL)	119 ± 32	120 ± 33
hs-CRP (mg/dL)	0.1 [0.0-0.2]	0.1 [0.1-0.2]

Note: Data are presented as mean ± standard deviation, median [interquartile range], or number (%).
Abbreviations: BMI, body mass index; eGFR, estimated glomerular filtration rate; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; hs-CRP, high-sensitivity C-reactive protein



Supplemental Figure 1. Graphical evaluation of the proportional hazards assumption using scaled Schoenfeld residuals in univariable Cox proportional hazards models for the association of chronic kidney disease with the frequency of secondhand smoke exposure

Note: *P*-value for slope = 0.93. Dots represents Schoenfeld residuals. Solid line is a smoothing spline fit to the plot with the dashed lines representing a 2-standard error band around the fit.



Supplemental Figure 2. Causal diagram showing assumed associations between baseline secondhand smoke, chronic kidney disease, and baseline characteristics. Variables with white circles are considered to be confounders and those with blue circles are considered to be effect mediator.

Note: Constructed with http://www.dagitty.net.
Abbreviations: BP, blood pressure