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Association of Dietary Potassium Intake with the Development of Chronic Kidney Disease and Renal Function in Patients with Mildly Decreased Kidney Function: The Korean Multi-Rural Communities Cohort Study

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

ABCDEF 1 Kwang Ho Mun
C 1 Gyeong Im Yu
BG 2 Bo Youl Choi
B 2 Mi Kyung Kim
B 3 Min-Ho Shin
ADG 1 Dong Hoon Shin

1 Department of Preventive Medicine, Keimyung University School of Medicine, Daegu, South Korea
2 Department of Preventive Medicine, Hanyang University College of Medicine, Seoul, South Korea
3 Department of Preventive Medicine, Chonnam National University Medical School, Gwangju, South Korea

Corresponding Author: Dong Hoon Shin, e-mail: dhshin@gmail.com
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Background: Dietary potassium has negative outcomes in patients with mildly impaired kidney function, while having positive outcomes in patients with hypertension. The association of dietary potassium intake with chronic kidney disease (CKD) development, with presence of hypertension, was studied in the Korean rural population with mildly impaired kidney function.

Material/Methods: From 3 rural areas of Korea, 5064 participants age ≥40 with CKD stage 2 at baseline were recruited. Patients were classified according to the quartile of dietary potassium intake. Newly developed CKD, defined as estimated glomerular filtration rate (eGFR) of <60 mL/min/1.73 m^2 at the time of follow-up, and eGFR decline, defined as eGFR decrease >15% at follow-up, were studied. The effect of dietary potassium on CKD development and eGFR decline were studied by Cox proportional hazard models. The association of potassium with blood pressures and C-reactive protein was also studied to examine the underlying mechanisms.

Results: Compared to 8.6% in normotensives, 15.7% of hypertensives developed CKD. The hazard ratio (HR) (95% confidence interval) of CKD was lower in high potassium diet only in hypertensives, with 0.60 (0.37-0.99) in the highest quartile. The eGFR decline was also lower in patients with higher potassium diet, with 0.70 (0.50–0.98) in Q3 and 0.54 (0.34–0.85) in Q4. Potassium intake has also been shown to decrease high diastolic blood pressure development (>90 mmHg) in hypertensives at 0.45 (0.25–0.83).

Conclusions: Dietary potassium was associated with lower risk of CKD development and eGFR decline, and this association was observed only in hypertensives.

MeSH Keywords: Cohort Studies • Kidney Failure, Chronic • Potassium, Dietary

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Background

The causes of chronic kidney disease (CKD) include obesity, diabetes, and hypertension [1–3]. Moreover, CKD increases risk of stroke, myocardial infarction, and mortality in the elderly [4]. In Korea, the prevalence of CKD is 8.2% according to Korean National Health and Nutrition Examination Survey (KNHANES), and 1572 patients undergo dialysis or renal transplantation per million population [5,6]. Therefore, early prevention and intervention of CKD development is critical to reduce the disease burden.

Potassium plays a variety of important roles in human physiology. According to the 2007–2010 KNHANES study, the average intake of potassium was 3081.9±16.8 mg per day, which is 74–83% of the recommended dietary intake [7]. A major role of dietary potassium intake is to decrease blood pressure in both hypertensive and normotensive individuals, and the effect is greater among hypertensives [8,9]. Increased potassium intake also improves endothelial function as assessed by flow-mediated dilatation [10]. The positive effects of potassium in the general population have been shown, without adverse effects on blood lipid and catecholamine levels, with lower risk of stroke, cardiovascular events, and mortality [11,12]. These results were consistent in hypertensive patients [13,14].

Compared to the general population, in CKD patients, as serum potassium level is balanced via excretion in functioning nephrons, hyperkalemia occurs [15]. As hyperkalemia is associated with increased mortality in CKD patients, restriction in dietary potassium is recommended in CKD patients [16,17].

Traditionally, stage 2 eGFR level is not considered CKD, as most epidemiologic studies use eGFR stage 3–5 to define CKD. However, studies have shown an association between eGFR and poor clinical outcomes, even within normal levels. An eGFR drop of 10 mL/min/1.73 m^2 was reported to increase odds of CVD and all-cause mortality, even in patients with eGFR 60 or higher [18]. Also, patients in stage 2, as well as stage 3, were associated with increased risk of CVD and mortality compared to patients with eGFR stage 1 [19]. These findings suggest the difference in the physiological effect of potassium between stage 2 *vs.* stage 1 patients.

This study, therefore, was conducted to examine the association of dietary potassium with CKD development in patients with mildly decreased kidney function, and to investigate whether the association differs according to hypertension status.

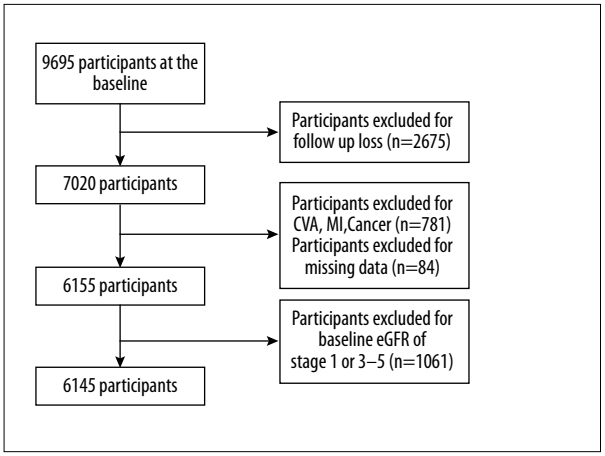

Figure 1. Flow chart of the study subjects. Missing data include creatinine, smoking, drinking, exercise, height, weight, and dietary factors. CKD – chronic kidney disease; CVA – cerebrovascular disease; eGFR – estimated glomerular filtration rate; MI – myocardial infarction.

Material and Methods

Study Population

The study patients were drawn from the Multi-Rural Communities Cohort (MRCohort), a cohort established in 2004 as part of the Korean Genomic and Epidemiology Study. The cohort was designed to study the risk factors of CVD in the Korean population. The study populations were from 3 rural centers in South Korea: Goryeong, Yangpyeong, and Namwon. Through multistage cluster sampling, villages were chosen and participants aged ≥40 years were recruited.

A total of 9695 participants were recruited as of 2009. Participants were then followed up every 2–4 years. By 2013, 7020 participants were followed up with data on eGFR.

The study participants were selected as shown in Figure 1. Among the participants, 2675 without follow-up data were excluded, as were 781 participants with cancer, cerebrovascular disease, or myocardial infarction. We also excluded participants with implausible dietary intake data (<500 or >4000 kcal/day or >10 missing food items in the survey) those without data from self-report surveys, including smoking, alcohol consumption, and exercise. Participants without laboratory data, such as serum creatinine, total cholesterol, triglyceride, or other confounding variables, such as body mass index (BMI) and blood pressure, were excluded. Lastly, participants with baseline estimated glomerular filtration rate (eGFR) higher than 90 or lower than 60, corresponding to stage 1 and 3, were also excluded from the analysis. Thus, 5064 participants were studied in the final analysis. This study was conducted with the approval of the Ethics Committee of Keimyung University in Korea (IRB No. 40525-201807-HR-65).

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Table 1. Demographics of the participants by hypertension at the baseline.

	Normotensive	Hypertensive	p
n	3066	1971	
CKD onset n (%)	265 (8.6%)	310 (15.7%)	<0.001
eGFR (mL/min/1.73 m2)	75.81±7.50	73.82±7.71	<0.001
Age (year)	59.9±9.2	62.7±8.5	<0.001
Men n (%)	1140 (37.2%)	749 (38.0%)	NS
Follow-up period (months)	46.7±18.8	47.8±19.6	<0.05
Smoker n (%)	439 (14.3%)	220 (11.2%)	<0.001
Alcohol n (%)	1319 (43.0%)	897 (45.5%)	<0.01
Exercise n (%)	900 (29.4%)	638 (32.4%)	<0.05
Diabetes n (%)	261 (8.5%)	281 (14.3%)	<0.001
BMI (kg/m^2)	23.9±3.0	25.1±3.1	<0.001
SBP (mmHg)	116.3±11.5	137.3±16.7	<0.001
DBP (mmHg)	75.2±7.7	85.1±10.4	<0.001
Tchl (mg/dL)	197.6±35.4	204.2±36.3	<0.001
TG (mg/dL)	139.7±85.2	169.7±108.6	<0.001
HDL (mg/dL)	45.0±10.4	43.9±10.3	<0.001
CRP (mg/L)	1.67±4.51	1.84±3.51	NS
Calorie (kcal/day)	1609.1±474.0	1580.3±455.6	<0.05
Protein (g/day)	48.5±19.2	47.5±19.1	NS
Potassium (mg/day)	1914.9±873.7	1889.7±918.4	NS
Sodium (mg/day)	2414.8±1347.7	2424.0±1408.8	NS

BMI – body mass index; CKD – chronic kidney disease; CRP – c-reactive protein; DBP – diastolic blood pressure; eGFR – estimated glomerular filtration rate; HDL – high-density lipoprotein; HTN – hypertension; NS – not significant; SBP – systolic blood pressure; Tchl – total cholesterol; Tg – triacylglycerol. Continuous variables are expressed as mean ± standard deviation and categorical variables are expressed as frequency and percentage.

Data collection

Data were collected from 3 centers by standardized protocols for questionnaires and examination procedures. All of the interviewers and technicians were trained by the same personnel from the coordinating center. The questionnaire included information on demographics and lifestyle (e.g., age, gender, smoking, drinking, and exercise). Medical history of diseases such as hypertension, diabetes, cerebrovascular disease, myocardial infarction, and cancer were also collected by the questionnaire.

Anthropometric measurements were collected by a trained examiner. Height and weight were measured to the nearest 0.1 cm and 0.1 kg, with instruments zero-balanced before each measurement. BMI was calculated as weight divided by height squared. Blood pressure was measured at the right arm at heart level after 10 min of rest. Two consecutive measures were taken with at least a 5-min interval between measurements, using a standard mercury sphygmomanometer. We determined the mean value of systolic (SBP) and diastolic blood pressure. HTN was defined as blood pressure of >140/90 mmHg or use of antihypertensives, or diagnosis of HTN, reported during the survey.

Laboratory test

Laboratory data were collected by blood samples from participants after a minimum of 8-h overnight fasting. All of the data were obtained on the same day, within 12 h of collection. Triacylglycerol, total cholesterol, high-density lipoprotein (HDL), serum creatinine, C-reactive protein (CRP), and fasting glucose levels were obtained using an ADVIA 1650 Automated Analyzer (Siemens, New York, NY, USA).

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Table 2. Demographics of the normotensive participants by potassium quartile at the baseline.

	Q1 (<1301.940 mg/day)	Q2 (1301.940–1765.602 mg/day)	Q3 (1765.603–2364.251 mg/day)	Q4 (>2364.251 mg/day)	*p*
n	767	766	766	767	
CKD onset n (%)	98 (12.78%)	72 (9.40%)	54 (7.05%)	41 (5.35%)	<0.001
eGFR (mL/min/1.73 m^2)	74.76±7.48	75.93±7.66	76.05±7.34	76.49±7.43	<0.001
Age (year)	63.90±8.52	60.96±8.65	58.19±8.96	56.39±8.80	<0.001
Men n (%)	221 (28.81%)	268 (34.99%)	305 (39.82%)	346 (45.11%)	<0.001
Follow-up period (months)	45.73±18.38	47.12±19.05	47.08±18.87	46.76±19.02	NS
Smoker n (%)	96 (12.52%)	100 (13.05%)	100 (13.05%)	143 (18.64%)	<0.01
Alcohol n (%)	276 (35.98%)	320 (41.78%)	335 (43.73%)	388 (50.59%)	<0.001
Exercise n (%)	147 (19.17%)	193 (25.20%)	241 (31.46%)	319 (41.59%)	<0.001
Diabetes n (%)	64 (8.34%)	64 (8.36%)	76 (9.92%)	57 (7.43%)	NS
BMI (kg/m^2)	23.57±3.21	23.76±2.89	23.87±2.91	24.37±2.90	<0.001
SBP (mmHg)	116.74±11.83	116.29±11.42	116.29±11.50	115.73±11.26	NS
DBP (mmHg)	74.56±7.78	75.13±7.43	75.57±7.76	75.69±7.66	<0.05
Tchl (mg/dL)	198.56±36.78	199.17±35.71	195.98±34.74	196.52±34.39	NS
TG (mg/dL)	141.51±85.80	140.79±87.04	134.17±80.61	142.33±87.09	NS
HDL (mg/dL)	44.90±10.22	45.51±10.42	44.94±10.44	44.83±10.53	NS
CRP (mg/L)	1.82±4.81	1.52±3.04	1.68±4.43	1.67±5.42	NS
Calorie (kcal/day)	1229.94±306.63	1469.85±324.76	1704.84±346.44	2031.63±478.15	<0.001
Protein (g/day)	31.05±7.63	41.36±8.89	51.75±10.64	69.66±20.36	<0.001
Sodium (mg/day)	1340.93±626.33	2064.50±769.30	2521.61±945.42	3732.30±1538.58	<0.001

BMI – body mass index; CKD – chronic kidney disease; CRP – c-reactive protein; DBP – diastolic blood pressure; eGFR – estimated glomerular filtration rate; HDL – high-density lipoprotein; HTN – hypertension; NS – not significant; SBP – systolic blood pressure; Tchl – total cholesterol; Tg – triacylglycerol. Continuous variables are expressed as mean ± standard deviation and categorical variables were expressed as frequency and percentage.

Dietary assessment

Dietary intake data were obtained by use of the food frequency questionnaire (FFQ), containing 106 food items. The validity of the FFQ was evaluated previously [20]. For each food item, participants were asked to select their food consumption frequency by 9 categories (from "never or rarely" to 3 times/day) and usual size of intake by 3 categories. For seasonal food items, data on the duration of intake (3, 6, 9, and 12 months) was also obtained. Dietary nutrition intake, including dietary potassium intake, were obtained by calculating consumption of foods and dietary supplements.

Diagnostic definition

The CKD-Epi equation was used to obtain eGFR. The validity of the equation was studied and reported previously [21]. eGFR <60 mL/min/1.73 m^2, using age and serum creatinine at the follow-up, was used to define CKD development. Participants were followed up until CKD development or until the last follow-up was conducted.

SBP, DBP, and CRP increase were defined as an increase of each variable at the follow-up compared to baseline levels.

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Table 3. Demographics of the hypertensive participants by potassium quartile at baseline.

	Q1 (<1235.661 mg/day)	Q2 (1235.661–1711.273 mg/day)	Q3 (1711.274–2322.677 mg/day)	Q4 (>2322.677 mg/day)	*p*
n	492	491	491	492	
CKD onset n (%)	112 (22.72%)	79 (16.02%)	69 (14.02%)	50 (10.14%)	<0.001
eGFR (mL/min/1.73 m^2)	72.70±7.63	73.81±7.76	73.90±7.72	74.86±7.60	<0.001
Age (year)	66.08±7.97	63.42±7.84	62.30±8.25	59.16±8.38	<0.001
Men n(%)	144 (29.21%)	165 (33.47%)	214 (43.50%)	226 (45.84%)	<0.001
Follow-up period (months)	46.08±19.66	48.17±19.71	49.02±19.66	47.93±19.19	NS
Smoker n (%)	58 (11.76%)	42 (8.52%)	63 (12.80%)	57 (11.56%)	<0.01
Alcohol n (%)	189 (38.34%)	214 (43.41%)	231 (46.95%)	263 (53.35%)	<0.001
Exercise n (%)	110 (22.31%)	150 (30.43%)	167 (33.94%)	211 (42.80%)	<0.001
Diabetes n (%)	64 (12.98%)	64 (12.98%)	73 (14.84%)	80 (16.23%)	NS
BMI (kg/m^2)	24.67±3.16	25.21±3.12	25.16±2.87	25.36±3.24	<0.01
SBP (mmHg)	138.76±16.42	137.33±17.80	136.06±15.99	137.20±16.64	NS
DBP (mmHg)	84.21±11.00	84.19±10.22	84.87±10.13	87.06±10.13	<0.001
Tchl (mg/dL)	205.91±35.91	206.64±38.89	202.09±35.32	202.33±34.73	NS
TG (mg/dL)	167.49±96.31	177.59±125.78	166.23±113.06	167.47±96.56	NS
HDL (mg/dL)	43.14±8.90	44.38±10.67	43.81±10.85	44.42±10.57	NS
CRP (mg/L)	1.92±3.51	1.66±2.98	1.99±4.47	1.78±2.87	NS
Calorie (kcal/day)	1225.05±284.10	1447.35±298.77	1631.11±345.46	2017.74±451.35	<0.001
Protein (g/day)	30.62±7.02	40.32±7.81	49.28±10.11	69.68±20.19	<0.001
Sodium (mg/day)	1259.21±644.07	1958.29±759.80	2584.18±931.25	3897.52±1519.28	<0.001

BMI – body mass index; CKD – chronic kidney disease; CRP – c-reactive protein; DBP – diastolic blood pressure; eGFR – estimated glomerular filtration rate; HDL – high-density lipoprotein; HTN – hypertension; NS – not significant; SBP – systolic blood pressure; Tchl – total cholesterol; Tg – triacylglycerol. Continuous variables are expressed as mean ± standard deviation and categorical variables are expressed as frequency and percentage.

Statistical analysis

Dietary potassium intake levels were categorized into 4 groups using quartile cut-off points. Participants were then assigned to a hypertensive group or a normotensive group based on presence of hypertension.

Variables are expressed as mean ± standard deviation (SD) for continuous variables, while frequency and percentage are used for categorical variables. One-way analysis of variance and chi-square test were used to compare the differences between groups. The outcome was defined as the development of CKD. The Cox proportional hazard model was used to assess hazard ratio (HR) and 95% confidence intervals (CI), with the first quartile as the reference. In the crude model, no confounders were adjusted. In model 1, age, gender, BMI, smoking, and drinking were adjusted. In model 2, smoking, drinking, exercise, diabetes, total cholesterol, triacylglycerol, and HDL were further adjusted. Total calorie intake and protein, categorized by recommended amount, were further adjusted in model 3. Furthermore, the association of dietary potassium intake with SBP, DBP, and CRP increase, as well as follow-up SBP ≥140 mmHg, DBP ≥90 mmHg, and CRP ≥3 mg/L, were studied to clarify the mechanism of CKD development. In all of the analyses, p <0.05 was considered statistically significant. IBM SPSS Statistics 23.0 (IBM Corp., Armonk, NY, USA) was used for all statistical analyses.

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Table 4. Hazard ratios for risk of chronic kidney disease and eGFR decline according to quartiles of potassium in whole participants.

	Q2	*p*	Q3	*p*	Q4	*p*
	HR (95% CI)		HR (95% CI)		HR (95% CI)	
CKD development						
Crude	0.64 (0.52–0.79)	<0.001	0.50 (0.40–0.62)	<0.001	0.39 (0.30–0.50)	<0.001
Model 1	0.82 (0.67–1.01)	NS	0.73 (0.58–0.92)	<0.01	0.71 (0.54–0.92)	<0.01
Model 2	0.84 (0.68–1.03)	NS	0.75 (0.60–0.95)	<0.05	0.73 (0.56–0.95)	<0.05
Model 3	0.83 (0.66–1.05)	NS	0.72 (0.54–0.95)	<0.05	0.65 (0.45–0.94)	<0.05
eGFR decline						
Crude	0.83 (0.69–0.99)	<0.05	0.73 (0.60–0.87)	<0.001	0.54 (0.44–0.67)	<0.001
Model 1	0.90 (0.75–1.08)	NS	0.83 (0.69–1.01)	NS	0.67 (0.54–0.83)	<0.001
Model 2	0.90 (0.75–1.08)	NS	0.84 (0.70–1.02)	NS	0.67 (0.54–0.84)	<0.001
Model 3	0.90 (0.74–1.10)	NS	0.85 (0.67–1.07)	NS	0.69 (0.51–0.93)	<0.05

CI – confidence interval; CKD – chronic kidney disease; eGFR – estimated glomerular filtration rate; HR – hazard ratio; NS – not significant. Model 1 – for age (by every 10 years), gender, BMI, smoking, alcohol and exercise; Model 2 – Model 1 + diabetes, total cholesterol, triglyceride, and high-density lipoprotein; Model 3 – Model 2 + calorie (by recommended amount) and protein intake (by recommended amount).

Results

Both hypertensive and normotensive subjects were divided into 4 groups according to the quartile of dietary potassium intake. The patients were followed up for average of 47.8±19.6 months in hypertensive patients and 46.7±18.8 months in normotensive patients. Table 1 presents differences in baseline characteristics between normotensives and hypertensives. CKD development was higher in hypertensives (15.7%) compared to normotensives (8.6%). Age, follow-up period, alcoholic intake, exercise, diabetes, BMI, total cholesterol, and triacylglycerol levels were higher in hypertensives. Smoking, HDL, and dietary calorie intake were higher in normotensives. Tables 2 and 3 present baseline characteristics of each group. In hypertensive patients, age significantly decreased as dietary potassium intake increased, but BMI, calorie, protein, sodium, male gender, smoking, and drinking increased as dietary potassium intake increased, with the highest levels in Q1 (Table 2). In the normotensive group, age was younger in the higher dietary potassium intake groups. BMI, calorie and protein intake, male gender, smoking, and drinking increased in the high dietary intake groups (Table 3).

Table 4 shows the association of dietary potassium with CKD development and eGFR decline of 15% or more compared to the lowest quartile of potassium intake. The risk of CKD development decreased as dietary potassium increased in high levels (Q3 and Q4) with adjusted HR (95% confidence interval (CI)) of 0.72 (0.54–0.95) and 0.65 (0.45–0.94). eGFR decline also was lower in the highest dietary potassium intake quartile (Q4), with adjusted HR (95% CI) of 0.69 (0.51–0.93).

Tables 5 and 6 show the association of dietary potassium with CKD development and eGFR decline of 15% or more compared to the lowest quartile of potassium intake. The risk of CKD development decreased in the highest dietary potassium intake group (Q4), with an adjusted HR (95% CI) of 0.60 (0.37–0.99). The risk of eGFR decline also decreased as dietary potassium increased in all of the quartiles (Q2, Q3, Q4), with adjusted HR (95% CI) of 0.72 (0.53–0.97), 0.70 (0.50–0.98), and 0.54 (0.34–0.85), respectively, in hypertensives. However, the association was not significant in normotensives in any of the quartiles, including Q4, with adjusted HR (95% CI) of 0.82 (0.48–1.41) and 0.84 (0.56–1.25). There was heterogeneity of CKD development (p for heterogeneity <0.01) between normotensive and hypertensive subjects.

To clarify the mechanism of dietary potassium on CKD development and changes in CRP, systolic and diastolic blood pressure were studied and are shown in Tables 7 and 8. Table 7 presents mean and SD of CRP, systolic and diastolic blood pressure in baseline and follow-up, and differences between the follow-up and baseline values of each variable. In both groups, diastolic blood pressures at baseline and follow-up were higher among high dietary potassium intake groups, but the differences were not significantly different. In the hypertensive group, the change in systolic blood pressure was also lower among high dietary potassium intake groups.

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Table 5. Hazard ratios for risk of chronic kidney disease and eGFR decline according to quartiles of potassium in normotensive participants.

	Q2	*p*	Q3	*p*	Q4	*p*
	HR (95% CI)		HR (95% CI)		HR (95% CI)	
CKD development						
Crude	0.68 (0.50–0.92)	<0.05	0.52 (0.37–0.72)	<0.001	0.40 (0.27–0.57)	<0.001
Model 1	0.88 (0.65–1.20)	NS	0.79 (0.56–1.11)	NS	0.69 (0.47–1.01)	NS
Model 2	0.86 (0.63–1.16)	NS	0.79 (0.56–1.12)	NS	0.69 (0.47–1.01)	NS
Model 3	0.93 (0.66–1.31)	NS	0.84 (0.55–1.28)	NS	0.82 (0.48–1.41)	NS
eGFR decline						
Crude	0.85 (0.65–1.11)	NS	0.71 (0.53–0.94)	<0.05	0.50 (0.36–0.69)	<0.001
Model 1	0.97 (0.74–1.28)	NS	0.90 (0.67–1.20)	NS	0.67 (0.48–0.93)	<0.05
Model 2	0.95 (0.72–1.25)	NS	0.89 (0.66–1.19)	NS	0.66 (0.47–0.92)	<0.05
Model 3	1.05 (0.80–1.37)	NS	0.94 (0.68–1.29)	NS	0.84 (0.56–1.25)	NS

CI – confidence interval; CKD – chronic kidney disease; eGFR – estimated glomerular filtration rate; HR – hazard ratio; NS – not significant. Model 1 – for age (by every 10 years), gender, BMI, smoking, alcohol and exercise; Model 2 – Model 1 + diabetes, total cholesterol, triglyceride and high-density lipoprotein; Model 3 – Model 2 + calorie, protein, and sodium intake (all of diet were adjusted by recommended amount).

Table 6. Hazard ratios for risk of chronic kidney disease and eGFR decline according to quartiles of potassium in hypertensive participants.

	Q2	*p*	Q3	*p*	Q4	*p*
	HR (95% CI)		HR (95% CI)		HR (95% CI)	
CKD development						
Crude	0.65 (0.49–0.86)	<0.01	0.55 (0.40–0.74)	<0.001	0.42 (0.30–0.59)	<0.001
Model 1	0.77 (0.57–1.03)	NS	0.69 (0.51–0.94)	<0.05	0.64 (0.45–0.91)	<0.05
Model 2	0.79 (0.59–1.05)	NS	0.71 (0.52–0.96)	<0.05	0.66 (0.46–0.93)	<0.05
Model 3	0.78 (0.57–1.07)	NS	0.69 (0.47–1.01)	0.053	0.60 (0.37–0.99)	<0.05
eGFR decline						
Crude	0.64 (0.48–0.86)	<0.01	0.62 (0.47–0.83)	<0.01	0.43 (0.31–0.61)	<0.001
Model 1	0.70 (0.52–0.95)	<0.05	0.71 (0.53–0.96)	<0.05	0.56 (0.39–0.79)	<0.01
Model 2	0.71 (0.52–0.95)	<0.05	0.72 (0.53–0.97)	<0.05	0.59 (0.40–0.80)	<0.01
Model 3	0.72 (0.53–0.97)	<0.05	0.70 (0.50–0.98)	<0.05	0.54 (0.34–0.85)	<0.01

CI – confidence interval; CKD – chronic kidney disease; eGFR – estimated glomerular filtration rate; HR – hazard ratio; NS – not significant. Model 1 – for age (by every 10 years), gender, body mass index, smoking, alcohol and exercise; Model 2 – Model 1 + diabetes, total cholesterol, triglyceride and high-density lipoprotein; Model 3 – Model 2 + calorie, protein, and sodium intake (all of diet were adjusted by recommended amount).

Table 8 shows the association of dietary potassium with increase of blood pressures and CRP. In normotensives, no association was observed. However, in hypertensives, DBP ≥90 mmHg at the follow-up decreased with high dietary potassium intake of adjusted HR (95% CI) of 0.45 (0.25–0.83).

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Table 7. Comparison of blood pressure and CRP from baseline to the follow-up by potassium quartiles.

	Q1	Q2	Q3	Q4	*p*
Normotensives					
SBP (mmHg)	116.69±11.79	116.37±11.48	116.25±11.52	115.73±11.25	NS
F/u SBP (mmHg)	117.16±14.79	117.01±14.51	116.73±14.04	115.77±14.04	NS
SBP difference (mmHg)	0.47±14.76	0.64±13.96	0.48±13.27	0.04±13.11	NS
DBP (mmHg)	74.57±7.75	75.07±7.50	75.64±7.73	75.63±7.67	<0.01
F/u DBP (mmHg)	71.37±8.84	71.61±9.26	72.28±8.96	72.36±9.41	<0.05
DBP difference (mmHg)	–3.20±9.40	–3.45±9.23	–3.37±8.79	–3.27±9.27	NS
CRP (mg/L)	1.86±4.92	1.48±2.93	1.67±4.42	1.67±5.38	NS
F/u CRP (mg/L)	1.93±7.11	1.85±4.71	1.62±4.34	1.67±5.30	NS
CRP difference (mg/L)	0.07±7.77	0.37±4.93	–0.04±5.48	–0.00±7.42	NS
Hypertensives					
SBP (mmHg)	138.45±16.42	137.43±17.87	136.44±16.17	136.98±16.42	NS
F/u SBP (mmHg)	128.02±15.44	127.31±15.32	127.71±16.01	128.87±14.90	NS
SBP difference (mmHg)	–10.44±19.84	–10.11±20.29	–8.74±19.63	–8.11±18.92	<0.05
DBP (mmHg)	84.05±10.91	84.20±10.39	85.23±10.01	86.96±10.16	<0.001
F/u DBP (mmHg)	74.73±10.50	75.27±10.61	76.38±9.96	77.34±9.74	<0.001
DBP difference (mmHg)	–9.32±11.44	–8.93±11.31	–8.85±10.81	–9.62±10.50	NS
CRP (mg/L)	1.90±3.53	1.63±2.82	2.00±4.52	1.82±2.92	NS
F/u CRP (mg/L)	2.11±4.12	2.08±5.32	1.87±4.46	1.81±3.49	NS
CRP difference (mg/L)	0.21±4.75	0.46±5.85	–0.12±5.86	–0.01±4.31	NS

CRP – c-reactive protein; DBP – diastolic blood pressure; NS – not significant; SBP – systolic blood pressure. Variables are expressed as mean ± standard deviation.

Discussion

This study was performed to assess the association of dietary potassium with CKD development in the Korean rural population. Our study has demonstrated that high dietary potassium intake of 2323 mg/day or more, compared to low intake of 1236 mg/day or lower, protected against CKD development in the hypertensive group, even after adjusting for nutritional factors. However, the association was insignificant in all quartiles of the normotensive group.

Decline in eGFR, even at normal levels, has been reported to be associated with poor clinical outcomes. It has been reported that every 10 mL/min/1.73 m^2 decrease in eGFR was associated with increased odds of CVD, recurrent CVD, and all-cause mortality, and the result was consistent in patients with eGFR higher than 60 [18]. A study by Ninomiya et al. demonstrated increased risk of CVD and mortality in patients with stage 2 and 3 [19]. The present study analyzed patients with stage 2eGFR because they are categorized as normal in most studies, but are relatively neglected despite the risk.

In the present study, the association of dietary potassium with CKD development was only significant in hypertensive patients and not in normotensive patients. This might result from the nature of hypertension. Hypertension is a traditional risk factor of CKD and its clinical outcomes. Improved cardiovascular and renal outcomes have been reported as SBP increases in stage 3–4 CKD patients [22]. Furthermore, other indexes of blood pressure, including DBP, pulse pressure, and mean arterial pressure, were also related to increased end-stage renal disease in patients with low eGFR [23]. Furthermore, in patients with decreased glomerular filtration rate, strict assignment of blood pressure has been shown to slow the progression of kidney disease [24]. In the present study, the decrease of systolic and diastolic blood pressure was greater in hypertensive patients with CKD development. Moreover, in hypertensives, the increase of diastolic blood pressure of 90 or higher decreased in the high dietary potassium group. This might have affected the differences in CKD development between patients. However, other factors, including systolic blood pressure or CRP, have failed to show a relationship with

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Table 8. Hazard ratios for risk of increase in blood pressures and CRP according to quartiles of potassium.

	Q2	*p*	Q3	*p*	Q4	*p*
	HR (95% CI)		HR (95% CI)		HR (95% CI)	
Normotensives						
F/u SBP ≥140	1.12 (0.74–1.69)	NS	1.07 (0.67–1.71)	NS	1.18 (0.66–2.12)	NS
SBP Increase	0.95 (0.82–1.10)	NS	0.90 (0.77–1.06)	NS	0.95 (0.78–1.16)	NS
F/u DBP ≥90	1.30 (0.70–2.43)	NS	0.79 (0.39–1.61)	NS	1.18 (0.39–1.61)	NS
DBP Increase	1.03 (0.90–1.17)	NS	1.09 (0.94–1.26)	NS	1.14 (0.95–1.35)	NS
CRP ≥3	0.88 (0.66–1.18)	NS	0.76 (0.54–1.07)	NS	0.69 (0.45–1.05)	NS
CRP Increase	0.97 (0.84–1.12)	NS	0.98 (0.84–1.16)	NS	0.97 (0.80–1.17)	NS
Hypertensives						
F/u SBP ≥140	1.02 (0.77–1.34)	NS	1.03 (0.76–1.39)	NS	1.35 (0.93–1.97)	NS
SBP Increase	0.89 (0.76–1.04)	NS	0.86 (0.73–1.02)	NS	0.94 (0.76–1.16)	NS
F/u DBP ≥90	0.88 (0.56–1.37)	NS	0.63 (0.39–1.03)	NS	0.45 (0.25–0.83)	<0.05
DBP Increase	0.91 (0.79–1.05)	NS	0.91 (0.78–1.07)	NS	1.08 (0.89–1.31)	NS
CRP ≥3	0.99 (0.71–1.38)	NS	0.69 (0.47–1.01)	NS	0.96 (0.60–1.55)	NS
CRP Increase	0.89 (0.74–1.06)	NS	0.84 (0.68–1.02)	NS	0.89 (0.69–1.14)	NS

CI – confidence interval; CRP – c-reactive protein; DBP – diastolic blood pressure; HR – hazard ratio; NS – not significant; SBP – systolic blood pressure. All models were adjusted for age (by every 10 years), gender, body mass index, smoking, alcohol, exercise, diabetes, total cholesterol, triglyceride, high-density lipoprotein calorie (by recommended amount), and protein intake (by recommended amount).

potassium intake. Therefore, further studies are needed to assess the effect of dietary potassium.

The underlying mechanisms causing potassium's association with low CKD development have not been clarified. However, studies have shown that a high potassium diet contributes to the incidence of stroke and cerebrovascular disease [8]. Several studies have also shown dietary potassium to decrease blood pressure [25–27]. In a meta-analysis, dietary potassium intake decreased systolic blood pressure of 3.5 mmHg in hypertensive patients, compared to 0.97 mmHg in normotensive patients [9]. Furthermore, potassium supplementation improved flow-mediated dilatation, a biomarker of endothelial function [28], and decreased levels of the inflammatory marker IL-8, but failed to show the effect of potassium in sensitivity analysis. Moreover, potassium has been reported to play a role in renal inflammation via Smad7 expression [29]. In the present study, dietary potassium levels were associated with reduced DBP increase to hypertensive levels. This might have resulted in the low CKD development in the present study, but we have failed to show an association between dietary potassium and SBP or CRP changes. Thus, the possible mechanisms by which potassium affects CKD development are diverse, and further studies are needed to clarify the effects of each mechanism.

There are some limitations to the present study. In defining CKD, albuminuria was not considered because the results were not available in the cohort. Regardless, eGFR of <60 mL/min/1.73 m^2 is widely accepted as defining CKD in epidemiologic studies [30]. Also, patients with stage 1 of eGFR were not analyzed in the present study, as few patients developed CKD, challenging the analysis of the population. This might be caused by the relatively short follow-up period of 47 months. Therefore, further follow-up is needed to compare the long-term effect between patients in stage 1 and stage 2. Lastly, we calculated dietary potassium levels by using food intake results from the FFQ. However, as FFQ obtains food consumption data over a relatively long period, recall bias might occur. Further studies should be conducted to gain more accurate dietary information.

Conclusions

In this study, high intake of potassium was found to protect against CKD development in hypertensive patients with mildly decreased kidney function. Further studies should be performed to compare the effect of dietary potassium in stage 1 and 2 hypertensive patients.

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