Association of plant protein intake and risk of incident chronic kidney disease: The UK Biobank study

Ga Young Heo[1], Hee Byung Koh[1], Chan-Young Jung[1], Hyung Woo Kim[1], Jung Tak Park[1], Tae Ik Chang[2], Tae-Hyun Yoo[1], Shin-Wook Kang[1], Seung Hyeok Han[1]
[1]Department of Internal Medicine-Nephrology, Severance Hospital, Korea, Republic of
[2]Department of Internal Medicine-Nephrology, National Health Insurance Service Ilsan Hospital, Korea, Republic of

Objectives: Dietary interventions have been considered important for chronic kidney disease (CKD) patients to slow disease progression and improve clinical outcomes. However, the association between plant protein intake and incident CKD is uncertain

Methods: Using the UK Biobank prospective cohort, we analyzed this association in 117,809 participants who completed more than one dietary questionnaire and had an estimated glomerular filtration rate (eGFR) ≥60 ml/min/1.73 m^2, urinary albumin-to-creatinine ratio (UACR) <30 mg/g, and no history of CKD. The main predictor was the daily plant protein intake, assessed with a web-based 24-hour recall questionnaire. The primary outcome was incident CKD based on the International Classification of Diseases, 10th Revision (ICD-10) or Office of Population Censuses and Surveys Classification of Interventions and Procedures, version 4 (OPCS-4) codes. We analyzed this association in 37,955 participants with primary care-linked data for eGFR and UACR. We used strictly defined CKD based on codes or two consecutive measures of eGFR <60 ml/min/1.73 m^2 or UACR >30 mg/g.

Results: During the median follow-up of 9.9 years, incident CKD occurred in 3745 (3.2%) participants (incidence rate, 3.2 per 1,000 person-years). In a multivariable cause-specific model, the adjusted hazard ratios (aHRs; 95% confidence intervals [CIs]) for the second, third, and highest quartiles were 0.91 (0.83-0.99), 0.79 (0.71-0.87), and 0.75 (0.64-0.85), respectively, compared with the lowest quartile. In a continuous model, the aHR (95% CIs) per 0.1 g/kg/day plant protein intake increase was 0.91 (0.88-0.94). This beneficial association was also consistent in the secondary analysis with strictly defined CKD and various sensitivity analyses.

Conclusions: This large, prospective cohort study showed that increased dietary plant protein intake was associated with a lower risk of CKD.

Table 1. Incidence rates of incident CKD according to quartile of plant protein intake

Outcomes	Total	Quartile of plant protein intake (g/kg/day)			
		Q1 (<0.28)	Q2 (≥0.28 and <0.35)	Q3 (≥0.35 and <0.45)	Q4 (≥0.45)
Total					
No. of participants	117809	29453	29452	29452	29452
Person-year	1168523	290582	291640	292755	293543
Incident chronic kidney disease					
Incidence of outcome, n (%)	3745 (3.2)	1155 (3.9)	1033 (3.5)	839 (2.8)	718 (2.4)
Incidence rate per 1000 person-years	3.2 (3.1-3.3)	4.0 (3.8-4.2)	3.5 (3.3-3.8)	2.9 (2.7-3.1)	2.4 (2.3-2.6)
Subcohort					
No. of participants	37995	9499	9499	9499	9498
Person-year	356709	87818	88698	89546	90646
Incident CKD (strictly defined)[a]					
Incidence of outcome, n (%)	2637 (6.9)	794 (8.4)	725 (7.6)	607 (6.4)	511 (5.4)
Incidence rate per 1000 person-years	7.4 (7.1-7.7)	9.0 (8.4-9.7)	8.2 (7.6-8.8)	6.8 (6.2-7.3)	5.6 (5.2-6.1)

[a] *Strict definition of CKD was defined as ICD codes in any primary care data, hospital inpatient data, and death register records or OPCS-4 codes in hospital inpatients data or two consecutive measurements of eGFR <60 ml/min/1.73 m², or UACR >30 mg/g, whichever came first*

Abbreviations: CKD, chronic kidney disease; ICD, ICD-10, International classification of diseases-10th revision; OPCS-4, Office of Population Censuses and Surveys Classification of Interventions and Procedures-version 4; eGFR, estimated glomerular filtration rate; UACR, urine albumin/creatinine ratio

Table 2. Associations of plant protein intake with incident chronic kidney disease

Plant protein intake	Model 1		Model 2		Model 3	
	HR (95% CI)	P value	HR (95% CI)	P value	HR (95% CI)	P value
Total (N = 117,809)						
Incident CKD						
Quartile						
<0.28 g/kg/day	1.00 (Reference)	-	1.00 (Reference)	-	1.00 (Reference)	-
≥0.28 and <0.35 g/kg/day	0.89 (0.82 - 0.97)	0.007	0.90 (0.82 - 0.98)	0.002	0.91 (0.83 - 0.99)	0.042
≥0.35 and <0.45 g/kg/day	0.72 (0.66 - 0.79)	<0.001	0.76 (0.69 - 0.85)	<0.001	0.79 (0.71 - 0.87)	<0.001
≥0.45 g/kg/day	0.62 (0.56 - 0.68)	<0.001	0.71 (0.63 - 0.80)	<0.001	0.75 (0.64 - 0.85)	<0.001
Continuous						
per 0.1 g/kg/day increase	0.87 (0.85 - 0.90)	<0.001	0.90 (0.87 - 0.93)	<0.001	0.91 (0.88 - 0.94)	<0.001
Subcohort (N = 37,995)						
Incident CKD (strictly defined)[a]						
Quartile						
<0.28 g/kg/day	1.00 (Reference)	-	1.00 (Reference)	-	1.00 (Reference)	-
≥0.28 and <0.35 g/kg/day	0.91 (0.82 - 1.00)	0.059	0.87 (0.78 - 0.97)	0.009	0.89 (0.80 – 0.99)	0.037
≥0.35 and <0.45 g/kg/day	0.75 (0.67 - 0.84)	<0.001	0.74 (0.65 - 0.84)	<0.001	0.78 (0.69 - 0.88)	<0.001
≥0.45 g/kg/day	0.64 (0.57 - 0.71)	<0.001	0.68 (0.59 - 0.78)	<0.001	0.73 (0.63 - 0.84)	<0.001
Continuous						
per 0.1 g/kg/day increase	0.88 (0.86 - 0.91)	<0.001	0.91 (0.87 - 0.95)	<0.001	0.92 (0.89 - 0.96)	<0.001

[a] *Strict definition of CKD was defined as ICD codes in any primary care data, hospital inpatient data, and death register records or OPCS-4 codes in hospital inpatients data or two consecutive measurements of eGFR <60 ml/min/1.73 m², or UACR >30 mg/g, whichever came first*

Note: Model 1: Without adjustment. Model 2: Model 1 + age, sex, BMI, ethnic background, socioeconomic status, alcohol status, smoking status, physical activity, dietary intake (total energy, total fat, total protein, total carbohydrate, and total sodium intake), and comorbidities (hypertension, diabetes, cardiovascular disease, chronic pulmonary disease, and liver disease). Model 3: Model 2 + the use of medications (renin-angiotensin-aldosterone system blockers, diuretics, and statins), and laboratory measurements (total cholesterol, LDL-C, triglyceride, and hs-CRP)

Abbreviations: CKD, chronic kidney disease; ICD, ICD-10, International classification of diseases-10th revision; OPCS-4, Office of Population Censuses and Surveys Classification of Interventions and Procedures-version 4; BMI, body mass index; LDL-C, low-density lipoprotein cholesterol; hs-CRP, high-sensitive C-reactive protein; eGFR, estimated glomerular filtration rate; UACR, urine albumin/creatinine ratio