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The Associations of Plant Protein Intake With All-Cause Mortality in CKD

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Abstract

Background—Plant protein intake is associated with lower production of uremic toxins and lower serum phosphorus levels. Therefore, at a given total protein intake, a higher proportion of dietary protein from plant sources might be associated with lower mortality in CKD.

Study Design—Observational study

Settings & Participants—14,866 NHANES III participants aged 20 years or older without missing data for plant and animal protein intake and mortality.

Predictors—Plant protein–total protein ratio and total plant protein intake. Patients were stratified by eGFR < or ≥ 60 ml/min/1.73 m².

Outcomes—All-cause mortality.

Measurements—Plant and total protein intakes were estimated from 24h dietary recalls. Mortality was ascertained by probabilistic linkage with National Death Index records through 12/31/2000.

Results—The mean of plant protein intake and plant protein–total protein ratio were 24.6 ± 13.2 (SD) g/d and 33.0% ± 14.0%, respectively. The prevalence of eGFR < 60 ml/min/1.73 m² was

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Contributions: Study concept and design: XC, SB, TG, TJ, JM; acquisition, analysis, or interpretation of data: all authors; statistical analysis: GW, TG; supervision: SB, TG, TJ, JM. Each author contributed important intellectual content during manuscript drafting or revision and accepts accountability for the overall work by ensuring that questions pertaining to the accuracy or integrity of any portion of the work are appropriately investigated and resolved. SB takes responsibility that this study has been reported honestly, accurately, and transparently; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned have been explained.

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4.9%. There were 2,163 deaths over an average follow-up of 8.4 years. Adjusted for demographics, smoking, alcohol use, comorbidity, BMI, calorie and total protein intake and physical inactivity, each 33% increase in plant protein–total protein ratio was not associated with mortality (HR, 0.88; 95% CI, 0.74–1.04) in the eGFR ≥ 60 mL/min/1.73 m² subpopulation, but was associated with lower mortality risk (HR, 0.77; 95% CI, 0.61–0.96) in the eGFR < 60 mL/min/1.73 m² subpopulation. In sensitivity analyses, results were similar in those with eGFR < 60 mL/min/1.73 m² defined by serum cystatin C.

Limitations—Whether the results are related to plant protein itself or to other factors associated with more plant-based diets is hard to establish.

Conclusions—A diet with higher proportion of protein from plant sources is associated with lower mortality in those with eGFR < 60 mL/min/1.73 m². Future studies are warranted to determine the causal role of plant protein intake in reducing mortality in those with eGFR < 60 mL/min/1.73 m².

Keywords

plant protein; animal protein; diet; protein intake; dietary recall; nutrition; chronic kidney disease (CKD); mortality; decreased renal function; estimated glomerular filtration rate (eGFR); disease progression; NHANES (National Health and Nutrition Examination Survey)

It is estimated that 14% of US adults have chronic kidney disease (CKD).¹ Mortality remains unusually high even in patients with non-dialysis-dependent CKD, with the annual rate surpassing 9% in patients with CKD stage 4.² Thus, CKD is extremely common, carrying a significant health burden. As high protein intake might accelerate CKD progression,³ the current national recommendations for dietary protein intake is 0.60 g protein/kg/d for individuals with CKD,^{4,p58} and 1.2 g protein/kg/d for clinically stable maintenance hemodialysis patients.^{4,p540} However, CKD patients tend to be at high risk for protein malnutrition because of their inadequate protein intake, acidemia-induced muscle breakdown, hyper-catabolism from a chronic inflammatory state, associated illnesses, and, when applicable, dialysis procedures.^{6–12} Thus, the optimal protein intake in individuals with non-dialysis-dependent CKD should minimize the risk of CKD progression, yet avoid malnutrition.

High-protein, plant-based diets have been investigated as an approach to decrease CKD progression as well as maintaining adequate nutrition. Some studies suggest that plant proteins do not accelerate CKD progression as animal proteins do. In the Nurses' Health Study,¹³ high animal protein intake in women with mild CKD was associated with significantly greater decline in estimated glomerular filtration rate (eGFR) than high plant protein intake. Furthermore, animal and human models suggest that plant protein diets may provide nutritional adequacy.^{14–18} In general healthy populations, studies found an inverse association between plant protein intake and all-cause mortality.^{19,20}

To our knowledge, the associations of plant protein with mortality in the CKD population have not been studied. Therefore, we hypothesized that at a given total protein intake, a higher proportion of dietary protein from plant sources is associated with lower risk of

mortality in CKD. We tested this hypothesis by examining the association of plant protein intake with all-cause mortality.

Methods

Study Population

The NHANES (National Health and Nutrition Examination Survey) III was conducted from 1988 to 1994 by the Centers for Disease Control and Prevention. The study design of NHANES was a multistage, stratified, clustered probability sampling of the United States' civilian population.²¹ NHANES III was approved by the Institutional Review Board at the Centers for Disease Control and Prevention, and written informed consents were obtained from all study participants.

Data on demographics (age, sex and race), history of comorbid conditions (myocardial infarction, stroke, congestive heart failure and cancer), current or past cigarette smoking, alcohol use (had at least 12 drinks in the last 12 months), and leisure-time physical inactivity (those with no self-reported leisure time physical activity) were collected in home interviews conducted by trained personnel. Anthropometric measurements, blood pressure readings, 24-hour dietary recall, blood and urine specimens, and other physical measurements were obtained at a mobile examination center.

In NHANES III, serum creatinine was measured using a kinetic rate Jaffe method, and recalibrated to standardized creatinine measurements obtained at the Cleveland Clinic Research Laboratory (Cleveland, Ohio) as standard creatinine $= (0.960 \times \text{serum creatinine}) - 0.184$.²² Kidney function was estimated by creatinine-based eGFR, calculated using the CKD-EPI (CKD Epidemiology Collaboration) creatinine equation²³.

Nutrition Intake Assessment

Dietary interviews were performed by an NHANES examiner in the mobile examination center for each subject. Dietary Data Collection System, a computer-based 24-h dietary recall program developed by the University of Minnesota's Nutrition Coordinating Center (NCC; Regents of the University of Minnesota), was used to assist the interviewer in the survey. The NHANES calculated the plant and animal protein intakes (variables "NCPNVPRO" and "NCPNAPRO")²⁴ using the US Department of Agriculture Survey Nutrient Database. The dietary recall data files were also coded to the NCC foods and nutrient composition database.²⁵ The NCC nutrient database has 165 nutrients, nutrient ratios and other food components, including total protein, animal protein and plant protein. Protein values were calculated from the analyzed nitrogen content of a food.²⁶ Plant protein is defined as the amount of protein contributed by plant products, including grains, fruits, vegetables, legumes, nuts and seeds. Animal protein sources include meats, eggs and dairy foods. The total protein in a food equals the sum of plant and animal protein in that food.²⁷ Details about dietary assessment methodology have been published elsewhere.²¹

Follow-up Data

The National Center for Health Statistics performed a probabilistic match between NHANES III and National Death Index death records to create a mortality file. Details about the NHANES III mortality linkage methodology have been provided elsewhere.²⁸ In this study, we used the follow-up mortality data from the date of survey participation (1988-1994) to December 31, 2000.

Statistical Analysis

As NHANES is based on a complex probability sample design, several aspects must be taken into account in data analysis. We used the svy suite of commands in Stata 12 (StataCorp LP, College Station, TX). Following the analytical guidelines for NHANES data, primary sampling units, pseudo strata ("SDPSTR6") and appropriate sampling weights were used to calculate the expected means and proportions of adults aged 20 and older in the US non-institutionalized civilian population.²⁹

Univariate descriptive statistics including means, standard deviations, and designated quantiles including medians, 25th and 75th percentiles were obtained for numeric variables; proportions were obtained to describe distributions of categorical variables.

Plant protein ratio was defined as plant protein–total protein ratio. In order to test whether a higher proportion of dietary protein from plant sources was associated with lower risk of mortality at a given total protein intake, we examined the mortality associations of plant protein ratio adjusted for total protein intake in eGFR ≥ 60 and < 60 mL/min/1.73 m² subpopulations in Cox regression models. These regression models were first adjusted for age, gender, race, smoking, alcohol use, calorie intake, and physical inactivity. In additional analyses, body mass index (BMI), hypertension, cancer, myocardial infarction (MI), congestive heart failure (CHF), stroke and diabetes were added as covariates. Calorie and fat intakes were highly correlated ($r = 0.87$). In order to avoid colinearity, only calorie intake was included in the models. In sensitivity analysis, fat intake was substituted for calorie intake.

In the above analyses, the hazard ratios (HRs) relating mortality to the plant protein ratio were expressed relative to a 33% increase in the plant protein ratio. We also examined the associations of quartiles of plant protein ratio with mortality using the lowest quartile as the reference.

To illustrate the shape of the relationship between the HRs of mortality and plant protein ratio, we also applied restricted cubic splines in Cox regression models with 4 knots and the 10th percentile of plant protein ratio as reference.

We evaluated whether the relationship between mortality and the plant protein ratio differed between the eGFR < 60 and ≥ 60 mL/min/1.73 m² subgroups by fitting the Cox regression analyses relating mortality to the plant protein ratio separately in the 2 eGFR groups, then computing the ratio of the difference in the Cox regression coefficients between the 2 groups to the standard error of this difference, and finally by comparing this ratio to quantiles of the standard normal distribution.

In sensitivity analyses, the associations of plant protein ratio with mortality in the subpopulation with cystatin C–based eGFR (eGFR_{cys}; calculated by the CKD-EPI cystatin C equation^{29a}) < 60 mL/min/1.73 m² as well as CKD stages 1 and 2 (eGFR ≥ 60 mL/min/1.73 m² and urinary albumin-creatinine ratio > 30 mg/g) were examined.

The assumption of proportional hazards was examined by comparing the logarithm of the HR for each predictor variable in the first 36 months of follow-up to the logarithm of the HR of the predictor variables after 36 months. No deviation from proportional hazards was detected with respect to plant protein ratio in any of the Cox regression models.

Results

The study population included 14,866 adult (≥ 20 years) participants with eGFR < 150 mL/min/1.73 m², with non-missing data for plant protein and total protein intake, as well as mortality status in those participants (Figure 1). The prevalence of eGFR < 60 mL/min/1.73 m² was 4.9%. The mean age was 44.8 ± 15.8 (standard deviation) years, 48% were men, and 10% were African Americans. The means of plant protein intake and plant protein ratio were 24.6 ± 13.2 g/d and 33.0% ± 14.0%, respectively.

Baseline characteristics by plant protein ratio quartiles in the entire cohort are summarized in table 1. Older age and presence of cardiovascular conditions (MI, CHF, or stroke) or lower eGFR were associated with higher plant protein ratio, whereas being male or African American, smoking, alcohol use and higher BMI were associated with a lower plant protein ratio. Those with higher plant protein ratio also had higher fiber and carbohydrate intake but lower total calorie, total fat, and saturated fat intake.

Out of 14,866 NHANES III participants included in the analysis, there were 2,163 deaths (14.6%) over an average follow-up of 8.4 years. The eGFR < 60 mL/min/1.73 m² subpopulation consisted of 1,065 participants with 633 deaths (59.4%) over an average follow-up of 6.2 years. The eGFR ≥ 60 subpopulation of 13,801 participants had 1,537 deaths (11.1%) over an average follow-up of 8.6 years.

After adjustment for age, gender, race, smoking, alcohol use, physical inactivity, and calorie intake, each 33% increase in the plant protein ratio had a statistically non-significant lower risk of death (HR, 0.87; 95% confidence interval [CI], 0.74-1.03) in the eGFR ≥ 60 mL/min/1.73 m² subpopulation but a significantly lower risk of death (HR, 0.81; 95% CI, 0.66-0.99) in the eGFR < 60 subpopulation (Table 2). These results were consistent in spline regression analyses in the eGFR ≥ 60 (Figure 2) and < 60 mL/min/1.73 m² (Figure 3) subpopulations. Further adjustment for BMI, hypertension, stroke, cancer, MI, CHF, and diabetes resulted in a stronger association of plant protein ratio with lower mortality in the eGFR < 60 mL/min/1.73 m² subpopulation but not in the eGFR ≥ 60 mL/min/1.73 m² subpopulation (Table 2). When these analyses were repeated with adjustment for fat intake instead of calories, each 33% increase in the plant protein ratio was not associated with mortality (HR, 0.88; 95% CI, 0.72-1.07) in the eGFR ≥ 60 mL/min/1.73 m² subpopulation, but with lower risk of death (HR, 0.79; 95% CI, 0.62-1.00) in the eGFR < 60 mL/min/1.73 m² subpopulation.

Compared to the lowest quartile of plant protein ratio (Table 2), the highest quartile had lower risk of mortality in the $\text{eGFR} < 60 \text{ mL/min/1.73 m}^2$ subpopulation (HR, 0.67; 95% CI, 0.46-0.96) but not in the $\text{eGFR} \geq 60 \text{ mL/min/1.73 m}^2$ subpopulation (HR, 0.89; 95% CI, 0.71-1.12; Table 2).

Regression coefficients relating plant protein ratio with mortality in the $\text{eGFR} \geq 60$ and $< 60 \text{ mL/min/1.73 m}^2$ subpopulations were not significantly different ($p > 0.05$) suggesting that reduced eGFR might not modify the associations of plant protein intake with mortality.

In sensitivity analyses, higher plant protein ratio was associated with lower mortality in those with $\text{eGFR}_{\text{cys}} < 60 \text{ mL/min/1.73 m}^2$ (Table 3) but not in those with CKD stages 1 or 2 ($\text{eGFR} \geq 60 \text{ mL/min/1.73 m}^2$ and urinary albumin-creatinine ratio $> 30 \text{ mg/g}$; Table 4).

Discussion

In the general population, the 2010 Dietary Reference Intake recommends an individual daily protein intake of 0.8 g/kg .³⁰ However, in the typical American diet, the average daily protein intake is approximately 1.2 g/kg .³¹ Popular weight-loss diets today recommend a high-protein, low-carbohydrate diet, which has been shown to promote weight loss in obese patients.³² Since obesity is a major risk factor for kidney damage,^{33,34} it might be reasonable to use a high protein diet in obese individuals for weight loss. On the other hand, there are concerns about whether a high protein diet poses particular problems for CKD patients, because high protein intake might cause nephrotoxicity and accelerate CKD progression.^{3,35,36}

The results of this study suggest that at a given total protein intake, a higher proportion of protein from plant sources is associated with lower mortality in CKD. The following discussion summarizes the current literature and interprets the current study.

Most studies on plant protein intake are food based, and thus cannot isolate the protein effect without considering other factors. However, various mechanisms have been proposed for the potential benefits of high plant protein intake in CKD.

The differences in amino acid composition of plant protein and animal protein might explain their different effects on kidney function. Individuals with high plant protein and low animal protein intake consume greater proportions of cysteine, proline, glutamic acid, phenylalanine, and serine, and smaller proportions of the other 13 amino acids versus individuals with lower plant protein and higher animal protein intake.³⁷

Plant proteins are also found to have a significant influence on cholesterol metabolism. High intakes of plant protein from gluten are shown to lower oxidized low-density lipoprotein (LDL) cholesterol, serum triacylglycerol, and uric acid.³⁸ Similarly, high intake of soy protein is found to significantly decrease serum total cholesterol, LDL cholesterol and triglycerides.³⁹ By decreasing these serum lipids levels, plant protein may help attenuate oxidized-lipoprotein-induced glomerular damage and CKD progression.⁴⁰

Another explanation for the benefits of plant protein involves the predominance of acid precursors in animal protein⁴¹ compared to the base precursors (e.g., potassium bicarbonate) found in plant protein.⁴² Imbalance between these precursors may cause a chronic net dietary acid load that contributes to complications and disease progression in CKD. In the African American Study of Kidney Disease and hypertension (AASK) cohort of more advanced CKD, results showed that a diet high in animal sources of protein may lead to higher estimated net endogenous acid production, which is associated with decreased serum bicarbonate⁴³ and greater loss of measured GFR.⁴⁴ In the same cohort, each 1-mmol/l increase in serum bicarbonate within the normal range was associated with decreased risk of a composite of death, dialysis, or GFR event.⁴⁵

A plant protein-rich diet is also associated with decreased production of uremic toxins such as *p*-cresyl sulfate and indoxyl sulfate,^{13,46} which have been implicated in CKD progression, cardiovascular disease, and mortality in kidney disease patients.⁴⁷⁻⁵¹ Since these uremic toxins accumulate in more advanced CKD, a diet high in plant sources might be more beneficial in preventing or managing advanced CKD.

In a Western diet, more than half of dietary phosphorus comes from animal proteins.⁵² Unlike the phosphorus in animal proteins, which is made up of organic phosphates, easily hydrolyzed and quickly absorbed, phosphorus in plant protein is mostly in the form of phytic acid or phytate.⁵³ Therefore, the bioavailability of phosphorus from plant food sources is fairly low (typically <50%).⁵⁴ In a crossover trial in nine CKD patients with a mean eGFR of 32 ml/min, 1 week of predominantly plant protein diet prepared by clinical research staff with nutrients equivalent to a meat diet led to decreased serum phosphorus levels and reduced fibroblast growth factor 23 levels.⁵⁵ Thus, theoretically, prescribing CKD patients a diet high in plant protein may not only meet their nutrition requirements but also lead to lower body phosphorus burden.

Despite plentiful evidence from observational research on the benefit of plant protein in decreasing cancer,⁵⁶⁻⁵⁸ cardiovascular mortality,^{19,20,56,59} blood pressure⁶⁰⁻⁶² and diabetes⁶³, caution is needed in interpreting these results. Whether the results are related to the plant protein itself or to the higher polyunsaturated fatty acid and lower saturated fatty acid or increased fiber levels associated with more plant-based diets is difficult to establish without intervention trials that increase solely plant protein. Therefore, even with observational studies suggesting benefit, such a result might not be seen in intervention trials.

There are other limitations to the current study. The eGFR was calculated based on a single measurement of serum creatinine, which may not account for changes in creatinine levels over time. Moreover, residual confounding due to unmeasured confounders cannot be ruled out. Finally, no method of dietary intake assessment is perfect. The misclassification of food sources may lead to underestimation or overestimation of the diet impact on mortality. In addition, a single 24-h-diet recall may not represent the usual or long-term dietary behavior of the patient. The 24-h-diet recall also has other disadvantages such as recall bias, patients being unable to remember everything, and difficulty estimating portion size and ingredients, etc. However, it provides good estimates of group means.

In conclusion, this study suggests that a higher proportion of protein from plant sources is associated with lower mortality in CKD patients.

Further studies should continue to explore different effects of plant protein and animal protein on kidney function, and establish the mechanisms of these associations. The causal role of plant protein in decreasing mortality in the CKD population should be established with intervention trials.

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Figure 1.
Participant flow chart

Figure 2.
Restricted cubic spline of mortality association of plant protein ratio in eGFR 60 mL/min/
1.73 m² subpopulation

Figure 3.
Restricted cubic spline of mortality association of plant protein ratio in eGFR < 60 mL/min/
1.73 m² subpopulation

Table 1

Baseline characteristics of entire cohort according to plant protein ratio quartiles

	Q1: <22.4% (n=3781)	Q2: 22.4%-30.6% (n=3611)	Q3: 30.7%-40.9% (n=3632)	Q4: >40.9% (n=3842)	P
Plant protein ratio (%)	16.6 ± 4.2	26.5 ± 2.1	35.3 ± 2.7	53.5 ± 11.4	
Plant protein intake (g/d)	16.6 ± 8.3	22.7 ± 10.2	26.7 ± 12.0	32.5 ± 16.5	<0.001
Total protein intake (g/d)	101.9 ± 47.8	85.9 ± 38.3	76.0 ± 34.2	62.5 ± 30.9	<0.001
Age (y)	42.6 ± 15.0	43.7 ± 15.3	45.8 ± 16.2	46.8 ± 16.7	<0.001
Male sex	53.5	48.6	44.8	43.4	<0.001
African American	14.1	11.2	9.4	8.0	<0.001
MI	3.1	3.0	4.0	3.7	0.2
CHF	1.7	1.7	2.4	2.7	0.02
Stroke	1.2	2.1	2.4	2.1	0.05
Diabetes mellitus	7.4	7.0	6.8	7.3	0.9
Cancer	3.8	2.5	4.2	4.9	0.002
Current smoker	36.3	31.5	24.7	20.6	<0.001
Alcohol use	59.9	54.7	52.1	48.8	<0.001
BMI (kg/m ²)	26.9 ± 5.4	26.6 ± 5.1	26.6 ± 5.3	26.1 ± 5.0	0.001
Leisure-time physical inactivity	14.5	15.6	14.1	14.9	0.7
Calorie intake (kcal/d)	2289 ± 1069	2266 ± 1005	2184 ± 939	2032 ± 901	<0.001
Saturated fat intake (g)	32.7 ± 19.7	30.5 ± 17.8	27.3 ± 14.9	22.0 ± 13.3	<0.001
Carbohydrate intake (g)	234 ± 115	269 ± 119	279 ± 123	285 ± 126	<0.001
Fiber intake (g)	12.8 ± 7.2	16.1 ± 8.0	18.7 ± 9.3	22.1 ± 11.8	<0.001
Total fat intake (g/d)	94.3 ± 53.3	89.5 ± 47.9	83.1 ± 43.7	72.1 ± 42.5	<0.001
Animal protein intake (g/d)	83.8 ± 41.0	62.0 ± 28.2	48.2 ± 22.3	29.2 ± 17.0	<0.001
eGFR (ml/min/1.73m ²)	101 ± 20	100 ± 20	98 ± 20	97 ± 20	<0.001
eGFR < 60 ml/min/1.73 m ²	3.8	4.6	5.3	5.9	0.002
Urinary ACR 30 mg/g (%)	8.1	7.9	8.9	9.0	0.5

Note: Values for categorical variables are given as percentage; for continuous variables, as mean ± standard deviation.

Abbreviations: MI, myocardial infarction; CHF, congestive heart failure; eGFR, estimated glomerular filtration rate; ACR, albumin-creatinine ratio; BMI, body mass index; Q, quartile

Table 2

Associations of plant protein ratio with all-cause mortality in normal and eGFR < 60 mL/min/1.73 m² subpopulations in continuous and categorical models

	Model 1[*]	Model 2^{\$}	Model 3[#]
eGFR ≥ 60 subpopulation (n =14801)			
Continuous model: per each 33% increase in plant protein ratio	0.89 (0.75,1.04)	0.87 (0.74,1.03)	0.88 (0.74,1.04)
Categorical model			
Q1: < 22.3%	1.00 (reference)	1.00 (reference)	1.00 (reference)
Q2: 22.3% - 30.5%	0.93 (0.72,1.21)	0.98 (0.77,1.27)	0.98 (0.78,1.24)
Q3: 30.6% - 40.8%	1.04 (0.83,1.30)	1.00 (0.81,1.24)	0.99 (0.79,1.24)
Q4: >40.8%	0.87 (0.69,1.09)	0.87 (0.70,1.08)	0.89 (0.71,1.12)
eGFR < 60 subpopulation (n =1065)			
Continuous model: per each 33% increase in plant protein ratio	0.94 (0.77,1.14)	0.81 (0.66,0.99)	0.77 (0.61,0.96)
Categorical model			
Q1: < 24.4%	1.00 (reference)	1.00 (reference)	1.00 (reference)
Q2: 24.4% - 32.7%	0.96 (0.65,1.43)	0.86 (0.58,1.27)	0.80 (0.55,1.17)
Q3: 32.8% - 43.5%	1.12 (0.81,1.54)	1.00 (0.69,1.45)	0.93 (0.66,1.29)
Q4: > 43.5%	0.85 (0.61,1.20)	0.73 (0.50,1.06)	0.67 (0.46,0.96)

Note: Associations are given as hazard ratio (95% confidence interval).

eGFR, estimated glomerular filtration rate; Q, quartile

* Model 1: adjusted for total protein intake

^{\$} Model 2: Model 1 + age, gender, race, smoking, alcohol use, calorie intake and physical inactivity;

[#] Model 3: Model 2 + body mass index, hypertension, cancer, myocardial infarction, congestive heart failure, stroke and diabetes

Table 3

Associations of plant protein ratio with mortality in eGFR_{cys} < 60 mL/min/1.73 m² subpopulation in continuous and categorical models

	Model 1[*]	Model 2^{\$}	Model 3[#]
Continuous model: per each 33% increase in plant protein ratio	0.75 (0.58,0.96)	0.75 (0.60,0.94)	0.73 (0.58,0.92)
Categorical model			
Q1: < 25.3%	1.00 (reference)	1.00 (reference)	1.00 (reference)
Q2: 25.3% - 33.3%	1.05 (0.77,1.44)	1.01 (0.75,1.36)	0.96 (0.71,1.29)
Q3: 33.4% - 43.5%	1.05 (0.82,1.35)	1.02 (0.77,1.35)	0.98 (0.78,1.23)
Q4: >43.5%	0.69 (0.49,0.96)	0.70 (0.51,0.96)	0.67 (0.49,0.92)

Note: n=1543. Associations are given as hazard ratio (95% confidence interval).

eGFR_{cys}, cystatin C–based estimated glomerular filtration rate

* Model 1: adjusted for total protein intake

\$ Model 2: Model 1 + age, gender, race, smoking, alcohol use, calorie intake and exercise level;

Model 3: Model 2 + body mass index, hypertension, cancer, myocardial infarction, congestive heart failure, stroke and diabetes

Table 4

Associations of plant protein ratio with mortality in CKD stages 1 and 2

	Model 1[*]	Model 2^{\$}	Model 3[#]
Continuous model: per each 33% increase in plant protein ratio	0.70 (0.49,1.00)	0.85 (0.60,1.20)	0.79 (0.54,1.16)
Categorical model			
Q1: < 22.8%	1.00 (reference)	1.00 (reference)	1.00 (reference)
Q2: 22.8% - 31.7%	1.02 (0.58,1.77)	1.26 (0.75,2.14)	1.17 (0.68,2.00)
Q3: 31.8% - 41.3%	0.73 (0.41,1.31)	0.93 (0.54,1.59)	0.93 (0.51,1.72)
Q4: >41.3%	0.83 (0.49,1.42)	1.01 (0.58,1.77)	0.90 (0.49,1.66)

Note: n=1347. CKD stages 1 and 2 refers to persons with estimated glomerular filtration rate ≥ 60 mL/min/1.73 m² and urinary albumin-creatinine ratio >30 mg/g. Associations given as hazard ratio (95% confidence interval).

CKD, chronic kidney disease; Q, quartile

* Model 1: adjusted for total protein intake

^{\$} Model 2: Model 1 + age, gender, race, smoking, alcohol use, calorie intake and exercise level;

[#] Model 3: Model 2 + body mass index, hypertension, cancer, myocardial infarction, congestive heart failure, stroke and diabetes