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Proinflammatory Diets and Risk of ESKD in US Adults with CKD

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Key Points

- The association between a proinflammatory diet and kidney failure with replacement therapy is strongly mediated by systemic inflammation.
- Inflammation seems to be a reasonable target for potential preventive and therapeutic interventions in patients with CKD.

Abstract

Background Inflammation may affect long-term kidney function. Diet may play a role in chronic inflammation. We hypothesized that proinflammatory diets increase the risk of progression to kidney failure with replacement therapy (KFRT), and systemic inflammation is a mediator of the effect of diet on progression to KFRT.

Methods In the 1988–1994 National Health and Nutrition Examination Survey linked to the national ESKD registry, in adults with CKD (eGFR 15–59 ml/min per 1.73 m^2), aged ≥20 years, we calculated the Adapted Dietary Inflammatory Index (ADII) at baseline from a 24-hour dietary recall and an inflammation score (IS) using average of z scores of four inflammation biomarkers. We explored the association of the ADII and IS with risk of incident KFRT using Cox proportional model, adjusting for sociodemographics, physical activity, Framingham risk score, eGFR, and urinary ACR. We evaluated whether, and to what extent, IS mediated the effect of the ADII on KFRT incidence, using causal mediation analysis.

Results Of 1084 adults with CKD, 109 (10%) developed KFRT. The ADII was associated with increased risk of KFRT (relative hazard [RH] per SD increase (2.56): 1.4 [1.04–1.78]). IS was also associated with KFRT (RH: 1.12; 95% CI, 1.02 to 1.25). Approximately 36% of the association between the ADII and KFRT was explained by IS.

Conclusions Among adults with CKD, a proinflammatory diet was associated with risk of KFRT, and that association was partially explained by an increase in inflammatory markers. Dietary interventions that reduce inflammation may offer an approach for preventing KFRT.

Introduction

Many common diseases, including cancer, diabetes, and cardiovascular disease, are linked to chronic inflammation. Inflammation is also believed to play a role in the genesis of kidney injury and may affect long-term kidney function (1). Therefore, inputs that induce, potentiate, or worsen inflammation and can potentially lead to worsening of kidney disease should be identified.

Diet may play a role in chronic inflammation (2,3). Nutrients believed to have a proinflammatory effect, such as saturated fatty acids, trans fats, or sugar, have been linked to worsening kidney function in community studies (4–7). In contrast, nutrients such as fiber or n-3 polyunsaturated fatty acids (n-3 PUFAs) are thought to have an anti-inflammatory effect and have been associated with slower kidney function decline and lower risk of albuminuria (8,9). However, nutrients are not consumed in isolation but as part of an overall diet. Proinflammatory dietary patterns have been associated with increased severity and

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occurrence of various diseases such as asthma, cardiovascular disease, diabetes, and cancer in nutritional and epidemiologic studies (10–13). Therefore, studying the pro- and anti-inflammatory potential of diets in addition to single nutrients in kidney disease is worthwhile.

In a systematic review of available literature, Cavicchia *et al.* (14) proposed establishing weights for a dietary inflammatory index on the basis of a number of components. Using this information, Woudenbergh *et al.* (15) developed and validated the Adapted Dietary Inflammatory Index (ADII). Xu *et al.* previously found in a Swedish community-based cross-sectional study that the ADII is associated with kidney function, and C-reactive protein (CRP) may mediate this association (16). Therefore, we were interested in examining the longitudinal association between proinflammatory diets and risk of progression to kidney failure with replacement therapy (KFRT) in the US population. We investigated whether the ADII is associated with both biomarkers of inflammation and the incidence of KFRT in individuals with CKD and to what extent, if any, inflammation explains the association between a proinflammatory diet and KFRT incidence.

Materials and Methods
Study Design and Population
We conducted a national cohort study on the basis of participants in National Health and Nutrition Examination Survey (NHANES) III, a national probability survey of US noninstitutionalized civilians conducted between 1988 and 1994 by the Centers for Disease Control and Prevention's National Center for Health Statistics (NCHS). NHANES III is linked to the United States Renal Data System (USRDS) and National Death Index files (derived from death certificate records and linked on the basis of probabilistic techniques) that contain, respectively, information on participants diagnosed with KFRT and mortality follow-up data from the time of NHANES III participation until the end of 2008, the details of which are provided elsewhere (17,18). We chose the criteria for linkage defined for the USRDS records as being more stringent than the criteria defined for National Death Index records. The linkage eligibility variable (CMS_Medicare_Match) in the NCHS-CMS Medicare feasibility file was used, and participants were linked to the USRDS records if the linkage eligibility variable took the value 1 (*i.e.*, for linkage eligibility and linked). We dropped participants with missing dietary information from our analysis. To be eligible, participants had to be ≥20 years of age ($n=5061$), have stages 3–4 CKD (eGFR between 15 and 59 ml/min per 1.73 m^2; $n=1250$), have dietary information ($n=1189$), and not be pregnant ($n=1084$).

Measurement of Albuminuria and Kidney Function and Classification of CKD
Serum creatinine (sCr) measurements obtained using a kinetic rate Jaffé method in NHANES III were recalibrated to standardized creatinine measurements obtained at the Cleveland Clinic Research Laboratory (Cleveland, OH) as standard creatinine$=0.184 + 0.96\times$measured sCr (19). Random spot urine samples were obtained and frozen. Urine albumin was measured using a solid-phase fluorescence immunoassay, and urine creatinine was measured using the

modified Jaffé kinetic method in the same laboratory. eGFR was calculated through determination of sCr using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation (20). Albuminuria, which is calculated as the urinary albumin-to-creatinine ratio (UACR), is expressed as milligrams of albumin per gram of creatinine (mg/g Cr) using American Diabetes Association categories: normal (<30 mg/g Cr) and albuminuria (≥30 mg/g Cr) (21). We defined the stages of CKD at baseline according to the National Kidney Foundation Kidney Disease Outcomes Quality Initiative (NKF KDOQI) CKD classification (22) on the basis of the level of kidney function (eGFR) and presence or absence of kidney damage (albuminuria). CKD stages 3 and 4 were defined as 30–59 and 15–29 ml/min per 1.73 m^2, respectively.

ADII Score
Diet history was obtained using a 24-hour recall administered by a trained interviewer in the mobile examination center. Dietary interviews were administered to all examinees by a trained dietary interviewer in the mobile examination center. The nutrient intakes reported included nutrients from foods and beverages reported in the 24-hour dietary recall. The nutrient intakes do not include nutrients obtained from other sources (*i.e.*, nutritional supplements, antacids, medications, salt and seasonings added to prepared foods at the table, and plain unbottled drinking water). The food records were on the basis of the Nutrient Coordinating Center nutrient composition database (1996). An automated, microcomputer-based dietary interview and coding system known as the NHANES III Dietary Data Collection System was used to collect all NHANES III dietary recall data. We calculated the ADII score (15) by multiplying standardized energy-adjusted intakes of the various dietary components (total of 26 nutrients/food items) by their respective inflammation weights (14) and summed these values. The adjustment of the daily intake of macro- and micronutrients for total energy intake was done by regression analysis of the residual method (23) in order to reduce the between-person variation in dietary intake; we also excluded some nutrients that were not available in our records (quercetin, genistein, epicatechin, daidzein, and cyanidin). In the current study, we separated n-6 PUFAs into the potentially proinflammatory arachidonic acid (20:4n-6) and the neutral or anti-inflammatory linoleic acid (18:2n-6) (24,25).

Inflammatory Score
We considered four serum inflammatory markers: CRP, serum albumin, white blood cell count, and mean platelet volume. To increase the power for testing associations, we created a summary index for individual inflammatory markers by rescaling each individual biomarker to have a mean of zero and a SD of 1 so that normalized z scores were obtained for each biomarker (26). The z scores for serum measures of inflammation were averaged to create the respective inflammatory score (IS).

Sociodemographic and Clinical Measurements
Medical history and demographic data were collected through a standardized questionnaire conducted at

participants' homes followed by a medical examination and laboratory testing that occurred in a mobile examination center (27).

Sociodemographic factors were also assessed during the interview. Race and ethnicity was self-reported by participants and categorized as non-Hispanic White (NHW), non-Hispanic Black (NHB), Mexican American (MA), or other. Self-reported information on socioeconomic position (SEP; *i.e.*, education, income, and sex) were also included. Self-reported income was assessed using the poverty income ratio (PIR), which is a ratio of household income to the US household poverty level (27).

Diabetes (other than during pregnancy) was defined by self-report of the condition or measured hemoglobin A1C (HbA1C) ≥6.5% (28). Body mass index (BMI) was calculated using both weight and height with weight in kilograms divided by the measured height in meters squared.

Physical Activity

In this study, three levels of physical activity were defined: inactive, insufficiently active, and active. We defined the inactive group as those people with no reported leisure-time physical activity. The active group was defined as those people who met the recommended levels of physical activity (29) at the time of the study, *i.e.*, self-reported leisure-time moderate activity (metabolic equivalent for task ranging from 3 to 6) of five or more times per week or leisure-time vigorous activity (metabolic equivalent for task >6) three or more times per week. The insufficiently active group was defined as those people who were not inactive and did not meet the recommended levels of physical activity.

Assessment of Cardiovascular Risk

The Framingham risk score (30) (FRS) was used to investigate the risk of cardiovascular disease (31). The FRSs were calculated on the basis of the eight coronary risk factors, including age, sex, total cholesterol (TC), HDL cholesterol, systolic BP, treatment of hypertension, diabetes status, and cigarette smoking. Smoking status was categorized as "current," "past," or "never" (no prior) cigarette use. The cutoffs for calculating FRS were as follows: TC <160, 160–199, 200–239, 240–279, and ≥280 mg/dl; for systolic BP, the cutoffs were: <120, 120–129, 130–139, 140–159, and ≥160 mm Hg; and the cutoffs for HDL cholesterol were: <40, 40–49, 50–59, and ≥60 mg/dl (32). Ten-year percentage risk was calculated by total points (1 point=6%, 2 points=8%, 3 points=10%, 4 points=12%, 5 points=16%, 6 points=20%, 7 points=25%, ≥10 points >30%).

Onset of ESKD

The outcome, onset of KFRT (*i.e.*, initiation of maintenance dialysis or kidney transplantation), was defined as entry into the national ESKD Registry from the time of enrollment into NHANES III through December 31, 2008. KFRT data are available for those NHANES III participants who agreed to provide personal identification data to NCHS and who the NCHS was able to match with USRDS administrative records (33).

Statistical Analyses

Baseline characteristics of study participants were examined according to tertiles of the ADII using chi-squared tests for categorical variables and ANOVA for numeric variables. Our first analysis examined the association between the ADII and IS using linear regression in our study population. Data are expressed as regression coefficients (β) and 95% confidence intervals (CIs). We then fitted a Cox proportional hazards model to explore the association of the ADII with KFRT with the models incrementally adjusted for potential confounders (age in years [as a continuous variable], sex [men/women], race/ethnicity, poverty status [<2 PIR or ≥2 PIR], education, physical activity, FRS, albuminuria, and eGFR). We adjusted for sociodemographic variables as preferred dietary patterns vary by adult age, cultural factors, and socioeconomic status (SES). Lower financial means and living in certain communities may affect the ability of individuals to obtain a diet rich in fruits and vegetables. Studies of the food and low SES environment suggest that low-income individuals often live in neighborhoods where there are few full-service grocery stores and may not have easy access to transportation to allow for shopping at such stores in outlying areas (34). We adjusted the model for physical activity and FRS because physical activity improves metabolic risk factors and FRS is an index for cardiovascular disease (35). Because a healthy dietary pattern is associated with eGFR and albuminuria, we adjusted the model for both (36–38).

We wanted to investigate the link between inflammation and CKD progression—a topic still under debate. A mediation model was used to test the effect of inflammation in the association between the ADII and risk of KFRT by using a method described by Valeri and Vanderweele (39). This method accounts for covariates in the estimation for causal effects. The effects (both direct and indirect effects defined counterfactually) were estimated as hazard ratios using Cox regression. We used the product method as the outcome in our analysis was a rare event (10% by end of follow-up) (40). The total effect was computed as the product of the natural direct and indirect effects. The proportion mediated (PM) on the hazard ratio scale is defined as the ratio of the natural indirect effect to the total effect. With hazard ratios used to estimate the natural direct effect (NDE) and the natural indirect effect (NIE), the PM on the hazard ratio scale is:

$$PM = \frac{NDE(NIE-1)}{NDE \times NIE - 1}.$$

Adjusted dietary weights and balanced repeated replication weights accounting for linkage eligibility were produced by fitting a marginal model. These weights were then used in the survey procedures as the final weights following the analytical guidelines for NHANES III data (41,42).

Sensitivity Analyses

We carried out a sensitivity analysis to test the robustness of our findings. We ran a competing risk model (43) to model competing events to account for the competing risks of death and KFRT. All analyses were performed using SAS v9.4 (SAS Institute, Inc., Cary, NC).

Table 1.   Baseline characteristics of 1084 adults with CKD

| Characteristic | Mean±SD, Median (Q1–Q3), % | Tertiles of ADII (Mean±SD, Median [Q1–Q3]) (%) | | | P Value |
		Lowest (–2.68 to 1.18)	Middle (1.19–1.84)	Highest (1.85–3.07)	
Sociodemographic, %					
Age, yr	75.6±1.4	76.3±1.9	75.9±1.5	74.5±1.4	<0.001
20–49		4	*n<5*	*n<5*	
50–69		23	*n<5*	*n<5*	
≥70		74	78	77	
Men	47	64	44	34	<0.001
Race and ethnicity, %					0.21
Other	3	3	2	3	
Mexican American	9	6	9	11	
Non-Hispanic Black	19	16	16	24	
Non-Hispanic White	70	75	73	62	
Socioeconomic position (PIR ≤2 or education less than high school)	73	66	71	82	<0.001
Physical activity, %					0.38
Inactive and insufficient active	80	90	94	97	
Active	20	10	6	3	
Clinical					
Body mass index, kg/m^2	26.9±2.1	26.8±0.3	26.7±0.2	27.2±0.3	0.39
Total cholesterol, mg/dl	226.5±3.2	218.3±2.5	227.5±2.6	233.9±2.7	<0.001
Systolic BP, mm Hg	146.7±1.9	145.2±1.5	145.2±1.3	149.6±1.4	0.03
Glycated hemoglobin, %	6.1±0.9	5.9±0.1	6±0.1	6.3±0.1	<0.001
Total caloric intake, kcal/day	1696±6.1	1960.4±15.4	1508.3±8.6	1435.2±11.7	<0.001
C-reactive protein, mg/dl	0.7±0.3	0.7±0.1	0.7±0.1	0.6±0.3	0.5
Serum albumin, g/L	40±3.5	39.9±3.6	40.1±3.6	40±3.3	0.81
Mean platelet volume, fL	8.4±1.1	8.5±1.1	8.4±1.1	8.4±1	0.9
White blood cell count	7.5±2.7	7.4±2.8	7.5±2.6	7.7±2.4	0.22
eGFR, ml/min per 1.73 m^2	48.2±1.5	49.2±0.5	48.5±0.5	46.7±54.9	<0.001
Albuminuria, mg/g	16.1 (6.8–62.9)	15.5 (6.2–55.2)	15.2 (7.2–51.6)	17.5 (6.8–98.4)	0.69

n<5, the values are suppressed as the cell frequency is <5 per NHANES guidelines. ADII, Adapted Dietary Inflammatory Index.

Institutional Review Board Approval

This study was exempt from Institutional Review Board approval because there was no direct contact with the participants.

Results

Characteristics of Participants

The baseline characteristics of the 1084 participants are described in Table 1. The ADII score ranged from –2.68 to 3.07, with a median score of 1.4 (25th–75th percentile: 0.96–1.98). The mean age of the participants was 75.6 years, the proportion of women was 53%, 19% of participants were non-Hispanic Black, and 73% of participants had a low socioeconomic position (*i.e.*, PIR <2 or less than a high school education). The cardiometabolic risk profile values for the participants were 6% for mean glycated hemoglobin, 146.7 mm Hg for average systolic blood pressure, 226.5 mg/dl for TC, and 26.9 kg/m^2 for BMI. The mean level of eGFR was 48.2 ml/min per 1.73 m^2, and UACR was 16.1 mg/g. During a follow-up of 14 years (median follow-up time=9.8 years), 109 (10%) KFRT events occurred.

Association between Diet and KFRT

In the unadjusted Cox proportional hazards model, a one-SD increase in the ADII (2.56) was associated with a higher risk of KFRT (relative hazard [RH]=2.1; 95% CI, 1.57 to 2.85). The risk of KFRT was attenuated when the model was adjusted for age, sex, race and ethnicity, PIR, and education level [RH=1.71; 95% CI, 1.14 to 2.39]). On further adjustment for covariates such as physical activity, FRS, baseline eGFR, and UACR, the increase in risk of KFRT per SD of the ADII was 40% (95% CI, 1.04 to 1.78; Figure 1). Adjusting for HbA1C levels beyond adjusting for FRS showed similar results (data not shown).

Association of Dietary Inflammation with Inflammatory Markers

A one-SD increase in the ADII was associated with higher IS in the unadjusted model (β=0.27; 95% CI, 0.23 to 0.30). On adjustment for potential confounders, per SD increase in the ADII was still significantly associated with the IS (β=0.26; 95% CI, 0.22–0.31). A one-SD increase in the ADII was significantly associated with an increase in each of the independent markers of inflammation in the multivariable models (Table 2).

Inflammation as a Mediator of the Associations between Diet and KFRT

A one-SD increase in the ADII was related to a 60% (95% CI, 1.18 to 2.01) increased risk for KFRT, corresponding to the total effect of the ADII on KFRT. We observe significant
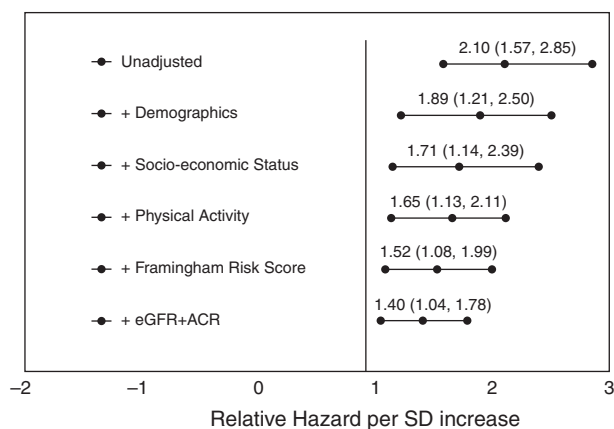
Figure 1. | Hazard ratio for the association between one-SD (2.56) increase in the Adapted Dietary Inflammatory Index (ADII) and the incidence rate of ESKD among 1084 adults with CKD.

direct and indirect effects of the ADII on KFRT (1.38 [1.07–1.69] and 1.16 [1.01–1.35], respectively) on the hazard ratio scale. The ADII displays a positive and significant association with inflammatory status in the multivariable model ($\beta=0.26$; 95% CI, 0.22 to 0.31). Inflammation is estimated to mediate 36% of the effect of the ADII on risk of KFRT (Table 3).

Sensitivity Analyses

The competing risk model yielded results similar to our primary analysis (Supplemental Table 1).

Discussion

In this national cohort study, we show that a proinflammatory diet (high in cholesterol and saturated fats) and relatively lacking in anti-inflammatory foods (fruits and vegetables) was associated with systemic inflammation and with risk of KFRT. This association was reduced but still significant even after adjusting for a range of potential confounding factors.

The mediating role of systemic inflammation in the association between the ADII and KFRT suggests that inflammation might be one of the pathways through which diet can affect kidney function. Chronic inflammation, as

Table 2. Unadjusted and adjusted association between the Adapted Dietary Inflammatory Index and log of each inflammatory marker z score or the combined inflammation z score

Marker or Score	Unadjusted Model	Adjusted Model[a]
C-reactive protein	0.02 (0.01, 0.03)	0.02 (0.002, 0.03)
Albumin level	0.05 (0.03, 0.10)	0.05 (0.03, 0.10)
Platelet volume	0.02 (−0.002, 0.03)	0.02 (0.002, 0.04)
White blood cell count	0.03 (0.02, 0.05)	0.03 (0.01, 0.05)
Inflammation score	0.27 (0.23, 0.32)	0.26 (0.22, 0.31)

[a]Adjusted for demographics, socioeconomic position, body mass index, physical activity, and Framingham risk score.

indicated by the continuous presence of serum inflammatory markers such as CRP, fibrinogen, and various interleukins, is a risk factor for numerous age-related, chronic disorders such as type 2 diabetes, cardiovascular disease, cancer, and metabolic syndrome (44,45) and increased frailty and cognitive decline (46). Kidneys play a central role in maintaining homeostasis in the body and can be the target of inflammatory, metabolic, and systemic vascular disorders (47). Nutrition and dietary patterns are implicated in the development of chronic metabolic diseases and are modifiable factors that can be utilized to prevent or slow the progression of CKD. Healthier diets (*e.g.*, rich in fruits and vegetables such as the Mediterranean diet) typically have been associated with lower inflammation levels, whereas Western-style diets (*e.g.*, high in fat and simple carbohydrates) have been associated with higher levels of inflammatory markers (48–51). Specific nutrients such as vitamins C, D, and E, β-carotene, n-3 PUFAs, flavonoids, and other dietary components such as fiber have been associated with lower levels of inflammation (2,52). In this study, as well, we found a proinflammatory dietary pattern to be significantly associated with markers of systemic inflammation in the CKD population.

We also found that higher ADII scores were associated with a range of unhealthy behavioral practices. Participants with a higher ADII score were more likely to be current smokers (data not shown) and less physically active. Smoking induces the release of proinflammatory markers, including IL-6 and acute-phase proteins, and decreases the production of anti-inflammatory cytokines (53). Although physical activity causes an acute-phase elevation of IL-6, in the long term, regular physical activity has an anti-inflammatory effect *via* multiple pathways, including cytokine production, improved endothelial function, and insulin sensitivity (54). Associations with BMI and SES were in line with similar research, although these were not statistically significant. Thus, higher ADII scores were found among those with a higher BMI and a lower SES in a population with a mean age of 75 years. The lack of a statistically significant association with BMI in this study is in contrast to many others that have examined the ADII in relation to BMI or obesity (14,55). There are two plausible explanations for this finding. First, by using BMI, we are examining the effect of overall obesity. However, other findings suggest that abdominal or central obesity (in both adults who have obesity and those who do not) is a specific contributor to inflammation (56,57). Second, the predictive ability of BMI changes over time. Obesity at midlife (related to the emergence of conditions such as hypertension) is related to higher risk of cardiovascular disease, dementia, and other outcomes but is not at older ages (58–61). In fact, high BMI in later life (>65 years of age) is a predictor of decreased morbidity and mortality.

Several limitations of our study should be considered. First, the ADII was determined using a single dietary recall questionnaire at baseline only rather than updated data on dietary intake and may not represent long-term habitual intake relevant to KFRT. Moreover, there is a high probability of participants misreporting/underreporting intakes of most reported foods and beverages because data were collected using self-reported dietary assessment instruments. This is likely the reason we observe the mean total caloric intake in the highest tertile of the ADII to be low

Table 3. Mediation analysis of the total effect of the Adapted Dietary Inflammatory Index on ESKD, decomposed into natural direct and indirect (mediated) effects, where the hypothesized mediator is the inflammation score[a]

Measure	Relative Hazard	95% Confidence Interval	P Value
Natural direct effect (NDE)	1.38	1.07 to 1.69	0.04
Natural indirect effect (NIE)	1.16	1.01 to 1.35	0.03
Total effect	1.60	1.18 to 2.01	0.03
Proportion mediated		$\frac{NDE(NIE-1)}{NDE \times NIE - 1} = \frac{1.38(1.16-1)}{1.38 \times 1.16 - 1} = 0.36$	

[a]The proportion of the total effect mediated by the inflammation score is 36%.

despite them having the highest HbA1C, BMI, and cholesterol levels. To account for this underreporting of food intake, we used the nutrient-residual model for estimating the ADII score. But the total caloric intake for all the participants was extracted from the 24-hour dietary recall, which is subject to measurement error. Confirming our findings in cohorts with repeated dietary assessments may be valuable. In addition, conducting future prospective studies with biomarkers of dietary intake will be advantageous in nutritional studies. Second, calculation of the ADII was on the basis of 21 of 26 food parameters, which may affect our findings. Despite these shortcomings, which would have increased overall error, we were able to detect a relationship between ADII and KFRT. Third, our study lacked follow-up data on laboratory values, including measures of kidney function. Thus, there is a possibility of misclassification of KFRT risk factors, such as diabetes, hypertension, eGFR, and ACR status that are defined from measurements at a single point in time. Fourth, a possibility of residual confounding exists. Changes in the inflammatory potential of diet over time were not accounted for because only baseline dietary data were used to calculate the ADII. There are many factors that determine serum concentrations of CRP, albumin, and other markers of inflammation, such as medical conditions and medications. We modeled the data on all the available potential confounders but acknowledge the nonavailability of medications data related to the pharmacologic treatment of inflammation in the current study. Fifth, we observed a large residual excess risk that could possibly be explained on the basis of single-point measurement of exposures in NHANES III. In particular, factors such as blood pressure, diabetes, lipid levels, eGFR, and UACR measured only at baseline could result in an underestimation of the strength of the attenuation between a higher ADII and KFRT. In assessing SES by using education and poverty levels, we might have inadequately adjusted for the local environment or access to and quality of health care. It is possible that these factors in combination could account for all of the residual excess risk among participants with a higher ADII. Sixth, both diet and IS were measured at the same point in time, and we do not expect a high IS to cause a diet to be proinflammatory. Seventh, our results may have been influenced by unmeasured confounders (*e.g.*, genetic differences, pulse pressure, heart failure, access to a nephrologist, health service decision making, patient preference related to commencement of KFRT). Lastly, as is the case for all observational analyses, causality cannot be inferred. These limitations are, however, counterbalanced by several strengths of the study, which include a large sample size, nationally representative study population, and long-term follow-up. The extended duration of the follow-up allowed us to study moderately long-term effects. Unlike previous studies (62–64) examining the association between dietary pattern and kidney disease, we had outcome data on the occurrence of KFRT, a consequential end point in CKD progression.

Our study findings showed a higher ADII (reflective of a proinflammatory dietary pattern) to be strongly associated with systemic inflammation. Thus, inflammation seems to be a reasonable target for potential preventive and therapeutic interventions in patients with CKD. The potentially deleterious effect of proinflammatory diets on kidney health, supported by our findings and those of other investigators, suggests the potential utility of the modulation of inflammatory properties of diets in strategies to prevent kidney disease. If confirmed in clinical trials, this knowledge may have application for both population-wide and high-risk approaches to CKD prevention and management in various settings.

Supplemental Material

This article contains the following supplemental material online at http://kidney360.asnjournals.org/lookup/suppl/doi:10.34067/KID.0000442022/-/DCSupplemental.

Supplemental Table 1. Hazard ratio for the association between one-SD (2.56) increase in the Adapted Dietary Inflammatory Index (ADII) and the incidence rate of KFRT among 1084 adults with CKD, using a competing risk model.

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