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Association between Dietary Inflammatory Index and kidney stones in US adults: data from the National Health and Nutrition Examination Survey (NHANES) 2007–2016

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Abstract

Objective: We evaluate the association between the Dietary Inflammatory Index (DII) and kidney stones.

Design: We performed a cross-sectional analysis using data from National Health and Nutrition Examination Survey (NHANES). Dietary intake information was assessed using first 24-h dietary recall interviews, and the Kidney Conditions were presented by a questionnaire. The primary outcome was to investigate the association between DII and incidence of kidney stones, and the secondary outcome was to assess the association between DII and nephrolithiasis recurrence.

Setting: The NHANES, 2007–2016.

Participants: The study included 25 984 NHANES participants, whose data on DII and kidney stones were available, of whom 2439 reported a history of kidney stones.

Results: For the primary outcome, after fully multivariate adjustment, DII score is positively associated with the risk of kidney stones (OR = 1·07; 95 % CI 1·04, 1·10). Then, compared Q4 with Q1, a significant 38 % increased likelihood of nephrolithiasis was observed. (OR = 1·38; 95 % CI 1·19, 1·60). For the secondary outcome, the multivariate regression analysis showed that DII score is positively correlated with nephrolithiasis recurrence (OR = 1·07; 95 % CI 1·00, 1·15). The results noted that higher DII scores (Q3 and Q4) are positively associated with a significant 48 % and 61 % increased risk of nephrolithiasis recurrence compared with the reference after fully multivariate adjustment (OR = 1·48; 95 % CI 1·07, 2·05; OR = 1·61; 95 % CI 1·12, 2·31).

Conclusions: Our findings revealed that increased intake of pro-inflammatory diet, as a higher DII score, is correlated with increased odds of kidney stones incidence and recurrence.

Keywords
Dietary Inflammatory Index
Kidney stones
National Health and Nutrition Examination Survey
Pro-Inflammatory diet

Kidney stone is a chronic disease, with a high prevalence of about 10 % around the world, and is correlated with high cost and morbidity[1,2]. The mechanisms of stone formation can only be identified in a few cases, where congenital abnormalities of the urinary tract or defined disorders of Ca and oxalate metabolism are discovered[3]. Otherwise, the main risk factors associated with kidney calculi are represented by poor fluid intake[4] and dietary imbalances, including excessive salt[5] and animal protein intake[6].

Diet patterns could be characterised by pro-inflammation or anti-inflammation. Different dietary interventions may impact the risk of kidney stone formation and recurrence. Dietary Inflammatory Index (DII) was developed as a standardised scoring system to evaluate the effects of diet on

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inflammation[7]. Currently, the DII approach to estimate the pro-inflammatory status of individual dietary intakes has been shown to link high DII scores with adverse health outcomes, such as general obesity[8], cancer[9] and CVD[10] in various general populations.

The role of nutrition in nephrolithiasis formation has been identified recently. Increased high-oxalate diet intake may significantly accelerate oxalate secretion[11], and high consumption of animal protein (like egg white) reduces urinary pH and elevates urinary uric acid[12], which are harmful elements for the development of Ca and uric acid stones. However, the mechanisms of how pro-inflammatory diet affects the immune system and inflammatory response in kidney stone formation are not fully understood. Some clinical researches noted that a high DII score has also been positively associated with increased levels of inflammatory markers such as TNF, IL-6 and C-reactive protein (CRP)[13]. Besides, experimental evidence in rats showed that some inflammatory cells like macrophages have been reported to facilitate kidney stones formation[14].

To our knowledge, relatively few researches have investigated a potentially inflammatory dietary pattern and kidney stones development. Therefore, our study aimed to evaluate the effect of DII on kidney stones using data from the US National Health and Nutrition Examination Survey (NHANES). We hypothesised that increasing inflammatory potential of dietary intake (i.e. higher DII scores) is associated with higher risk of kidney stones.

Materials and methods

Data source and study population

We performed an analysis using data from the NHANES, a periodic cross-sectional survey to monitor trends in the health and nutritional status of the non-institutionalised US civilian population conducted by the Centers for Disease Control and Prevention. The NHANES provides prevalence estimates for an array of common diseases by performing a complex, multistage, probability sampling design. For the present analysis, five survey cycles (i.e. 2007–2008, 2009–2010, 2011–2012, 2013–2014 and 2015–2016) were combined to produce estimates with greater precision and smaller sampling error. We only include non-pregnant participants aged 18–80 years (*n* 50 588). Then, we excluded participants without complete information on kidney stones (*n* 21 467) and dietary intake (*n* 3137). In total, 25 984 eligible individuals of the NHANES were included. The NCHS Research Ethics Review Board approved the study protocol of 2007–2010 (protocol 2005–2006) and 2011–2016 (protocol 2011–2017) NHANES, and all participants provided written informed consents[15].

Exposure and outcome definitions

Dietary intake information was assessed using the first 24-h dietary recall interviews. NHANES processed the dietary data to acquire micro- and macronutrient contents by using the USDA's Food and Nutrient Database for Dietary Studies that is specific for the years during which each of the 2-year cycles of NHANES was conducted. Shivappa *et al.* reported the development of the calculation of DII. 'Inflammatory effect scores' were evaluated from the peer-reviewed publications for forty-five DII food parameters which include nutrients, foods and bioactive compounds that were assessed based on their relation to six inflammatory cytokines (IL-1β, IL-4, IL-6 and IL-10) in addition to CRP and TNF-α[7]. In our analysis, twenty-seven of the forty-five food parameters were available to calculate DII, including energy, carbohydrate, fibre, protein, cholesterol, fat, SFA, MUFA, PUFA, niacin, vitamin B_6, vitamin B_{12}, Mg, Se, Zn, Fe, thiamin, riboflavin, vitamin A, vitamin C, vitamin D, vitamin E, beta carotene, folic acid, *n*-3, *n*-6 and alcohol. Previous studies have reported a stable predictive ability when only using twenty-eight food parameters[16]. The process of DII score calculation is presented in Supplementary material 1. Finally, all scores were summed from all food parameters to calculate the overall DII score. Higher numerical DII scores indicate a greater pro-inflammatory state of the diet, while lower numerical scores are consistent with anti-inflammatory diets[7]. The DII score was analysed as a continuous variable, and then we categorised into quartiles (Q1, Q2, Q3, Q4) from the total sample size.

The Kidney Conditions questionnaire was directed at adults aged 20 years and older, which includes questions about a history of nephrolithiasis from 2007 to 2016. The accuracy of self-reported kidney stones has been reported elsewhere; Curhan *et al.* have confirmed the validity of self-reported stones in the Health Professionals Follow-up Study by analysing medical records from a random sample of sixty men in the cohort. The chart review confirmed that 97 % of the cases reported kidney stone[17]. A similar study in the Nurses' Health Study I examined medical records from a random sample of ninety women who reported kidney stone. The records confirmed the diagnosis for all except 1 participant (98 %)[18]. Survey participants who answered yes to 'Have you/Has sample person (SP) ever had a kidney stone?' were considered to have a history of nephrolithiasis. A follow-up question was then asked: 'How many times have you/has SP passed a kidney stone?' We divided the participants into two groups, passed a kidney stone <2 times as well as ≥2 times. We interpret the latter to mean a recurrence of passing kidney stones

Covariates

Potential covariates were identified *a priori* based on a review of the literature[19,20]. The following confounders were summarised in multivariable-adjusted models: continuous variables consisted of age, poverty:income ratio, BMI, energy, categorical variables included gender (male/female), marital status (married or living with partner/single), race/ethnicity, insurance, education, smoking,

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alcohol intake per week, physical activity and co-morbidity index. Co-morbid conditions consisted of diabetes mellitus, congestive heart failure, coronary artery disease, chronic obstructive pulmonary disease (chronic bronchitis and/or emphysema), hypertension and cancer. The number of subject reported conditions was then combined to generate an ordinal co-morbidity index[19].

Statistical analysis

Statistical analysis was performed in accordance with CDC analytical reporting guidelines for complex NHANES data analysis (https://wwwn.cdc.gov/nchs/nhanes/tutorials/default.aspx). A sample weight was assigned to each person participating in the NHANES. Hence, we considered masked variance and used the recommended weighting methodology. Data are expressed as mean ± SD or proportions. To calculate for differences among different DII score groups (quartiles), statistical differences were determined using a weighted t test for continuous variables, while a weighted χ^2 test was used for categorical variables.

Our statistical analysis consisted of three main strategies to examine whether DII is associated with kidney stones. First, we employed weighted univariate which was simple and easy to interpret, and multivariate logistic regression models were then performed. We estimated the crude model (model 1) as well as model 2 (only gender; age and race were adjusted). In the final model (model 3), we further adjusted for BMI; poverty:income ratio; education level; insurance; marital status; alcohol intake per week; physical activity; co-morbidity index; energy (kcal) and smoking. Second, to account for the non-linear association between DII score and kidney stone, we performed a smooth curve fitting (penalised spline method) and a weighted generalised additive model regression. Third, to further determine the correlation between DII and kidney stones, we used weighted stratified logistic regression models to conduct subgroup analyses. In sensitivity analysis, we further excluded patients with stone disease related to metabolic abnormalities such as Crohn's disease, primary hyperparathyroidism and non-alcoholic fatty liver disease, as stone disease in this population may not be related to diet habitus.

All analyses were performed using the statistical software packages R (http://www.R-project.org; The R Foundation) and EmpowerStats (http://www.empowerstats.com, X&Y Solutions, Inc.). All P values <0·05 (two-sided) were considered statistically significant.

Results

Participants' baseline characteristics

Data on kidney stones as well as DII scores were available on 25 984 NHANES participants older than 20 years. The basic demographic characteristics and other covariates of the included participants in the NHANES 2007–2016 population, according to DII score quartiles, are summarised in Table 1. The participants in this sample averaged 49·41 ± 17·71 years old, with males representing 48·6 %. Mean ± SD DII score was 1·30 ± 2·00, with 9·4 % reporting a history of kidney calculi and 32·5 % of these experiencing recurrent kidney calculi.

Multivariate regression analysis

For the primary outcome, our multivariate regression analysis noted that DII score positively correlated with nephrolithiasis (OR = 1·07; 95 % CI 1·04, 1·10) (see Table 2). Q3 and Q4 had a significantly higher risk of nephrolithiasis than Q1 in the non-adjusted model (model 1, OR = 1·15; 95 % CI 1·02, 1·30; OR = 1·24; 95 % CI 1·10, 1·40), minimally adjusted model (model 2, OR = 1·24; 95 % CI 1·09, 1·40; OR = 1·40; 95 % CI 1·24, 1·58) and fully adjusted model (model 3, OR = 1·22; 95 % CI 1·06, 1·40; OR = 1·38; 95 % CI 1·19, 1·60), while there is no significant difference between Q1 and Q2. For example, compared Q4 with Q1, a significant 38 % increased likelihood of nephrolithiasis was observed (OR = 1·38; 95 % CI 1·19, 1·60). Furthermore, the risk of nephrolithiasis rose significantly stepwise across DII score quartiles ($P_{\text{for trend}} < 0·0001$). In sensitivity analysis, the positive association still remained significant after excluding patients with stone disease related to metabolic abnormalities (data not shown).

For the secondary outcome, multivariate regression analysis showed that DII score also positively correlated with nephrolithiasis recurrence (OR = 1·07; 95 % CI 1·00, 1·15) (see Table 2). After fully multivariate adjustment, the results noted that higher DII scores (Q3 and Q4) are positively associated with a significant 48 % and 61 % increased risk of nephrolithiasis recurrence compared with the reference (OR = 1·48; 95 % CI 1·07, 2·05; OR = 1·61; 95 % CI 1·12, 2·31). Furthermore, the risk of nephrolithiasis recurrence significantly increased stepwise when the DII score was classified as a categorical variable (quartiles) ($P_{\text{for trend}} = 0·0076$).

Nonlinearity analysis and subgroup analyses

We also analysed the non-linear relationship between DII and nephrolithiasis formation and its recurrence (see Fig. 1, Fig. 2). Then, in the multivariable models, no statistical significance was indicated by the interaction terms in the association between DII and kidney stone incidence. In stratified analyses for people with recurrent kidney stones, except for the physical activity, there was no statistically significant interaction effect after adjusting for covariates. With a 1 SD increase in DII score, the odds of recurrent nephrolithiasis among those with less than moderate, moderate and vigorous physical activity increased 10 % (1–20 %), 25 % (1–55 %) and –2 % (–10–8 %), respectively ($P_{\text{for interaction}} = 0·0375$) (see Table 3).

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Table 1 Characteristics of participants in the 2007–2016 continuous National Health and Nutrition Examination Survey*,†,‡

Characteristic	Total (*n* 25 984)	Q1 (*n* 6496)	Q2 (*n* 6496)	Q3 (*n* 6496)	Q4 (*n* 6496)	*P*-value
Age (years)						<0·001
Mean	49·41	48·68	49·16	49·56	50·22	
SD	17·71	17·04	17·47	17·84	18·42	
<60%	67·0	70·2	68·1	66·1	63·8	
≥60%	33·0	29·8	31·9	33·9	36·2	
Gender (%)						<0·001
Male	48·6	62·1	52·9	44·7	34·9	
Female	51·4	37·9	47·1	55·3	65·1	
Dietary inflammatory index						<0·001
Mean	1·30	–1·43	0·73	2·20	3·70	
SD	2·00	0·99	0·46	0·40	0·54	
Poverty to income ratio						<0·001
Mean	2·44	2·75	2·54	2·37	2·09	
SD	1·56	1·63	1·57	1·52	1·44	
<1·3%	30·0	24·6	27·2	30·7	37·7	
≥1·3and <3·5(%)	42·6	39·5	43·4	44·0	43·4	
≥3·5%	27·4	35·9	29·4	25·3	18·9	
Race/ethnicity (%)						<0·001
Mexican American	15·4	16·7	16·5	15	13	
Non-Hispanic Black	21·2	16·7	19·0	22·3	26·5	
Non-Hispanic White	42·7	44·0	43·1	42·0	44·0	
Other Hispanic	10·6	9·8	10·7	11·2	10·9	
Other race/ethnicity	10·2	12·8	10·6	9·4	7·8	
Education (%)						<0·001
Less than high school	24·2	19·4	21·9	25·5	30·2	
High school or GED	22·0	18·3	21·9	23·5	24·5	
More than high school	53·7	62·3	56·2	51·1	45·4	
Insurance (%)						<0·001
No	22·3	21·0	21·8	22·3	24·2	
Yes	77·7	79·0	78·2	77·7	75·8	
Marital status (%)						<0·001
Married or living with partner	63·4	67·4	66·0	62·5	57·6	
Single	36·6	32·6	34·0	37·5	42·4	
Alcohol intake per week (%)						<0·001
Never	17·2	14·1	15·9	17·8	21·1	
Up to once a week	63·2	59·4	62·8	63·5	66·9	
2–3 times a week	10·7	14·4	10·8	10·3	7·2	
4–6 times a week	5·1	6·9	6·1	4·7	2·7	
Daily or more	3·8	5·2	4·4	3·6	2·1	
BMI, mean ± SD (kg/m^2)						<0·001
<25	29·17	28·30	29·05	29·53	29·80	
≥25	6·90	6·37	6·77	7·04	7·27	
Energy (kcal)						<0·001
Mean	2093·64	2878·65	2260·49	1854·68	1380·75	
SD	995·59	1183·69	780·22	633·40	587·01	
Low	50·0	19·0	38·6	59·9	82·4	
High	50·0	81·0	61·4	40·1	17·6	
Physical activity (MET-based rank) (%)						<0·001
Less than moderate	52·8	41·7	50·4	56·9	62·1	
Moderate	9·5	9·6	10·1	9·6	8·8	
Vigorous	37·7	48·8	39·5	33·5	29·1	
Current or past cigarette smoker (%)						<0·001
None	55·4	57·1	56·1	55·1	53·1	
Former	27·8	30·7	29·2	27·3	24·3	
Current	16·4	12·2	14·7	17·6	22·7	
Co-morbidity index (%)						<0·001
0	57·3	24·6	27·2	30·7	37·7	
1,2	40·0	39·5	43·4	44·0	43·4	
3,4	2·6	35·9	29·4	25·3	18·9	
Kidney stones (%)						0·002
No	90·6	91·5	91·0	90·3	89·7	
Yes	9·4	8·5	9·0	9·7	10·3	
Kidney stones, times (%)						0·056
<2	67·5	73·0	66·4	65·2	66·2	
≥2	32	27·0	33	34·8	33·8	

DII, Dietary Inflammatory Index; GED, General educational development.
*Mean and SD for continuous variables: *P* value was calculated by weighted *t* test.
†% for Categorical variables: *P* value was calculated by weighted χ^2 test.
‡DII quartile ranges: Quartile 1 = –5·18 to–0·12; Quartile 2 = –0·12 to 1·50; Quartile 3 = 1·50 to 2·88, Quartile 4 = 2·88 to 5·48

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Table 2 Association of Dietary Inflammatory Index with kidney stones

	Passed a kidney stone (<2)												Passed a kidney stone (≥2)											
	Model 1 (*n* 25 984)*			Model 2 (*n* 25 984)†			Model 3 (*n* 25 984)‡						Model 1 (*n* 1861)*			Model 2 (*n* 1861)†			Model 3 (*n* 1861)‡					
Exposure	OR	95 % CI	*P* value	OR	95 % CI	*P* value	OR	95 % CI	*P* value				OR	95 % CI	*P* value	OR	95 % CI	*P* value	OR	95 % CI	*P* value			
Dietary inflammatory index§																								
Dietary inflammatory index	1·05	1·02, 1·07	<0·001	1·07	1·05, 1·09	<0·001	1·07	1·04, 1·10	0·001				1·04	0·99, 1·09	0·116	1·06	1·01, 1·12	0·028	1·07	1·00, 1·15	0·059			
Dietary inflammatory index (quartile)																								
Q1	1			1			1		1				1			1			1					
Q2	1·07	0·94, 1·20	0·306	1·10	0·97, 1·24	0·142	1·08	0·95, 1·23	0·217				1·36	1·02, 1·83	0·038	1·33	0·99, 1·79	0·059	1·31	0·96, 1·79	0·091			
Q3	1·15	1·02, 1·30	0·022	1·24	1·09, 1·40	0·006	1·22	1·06, 1·40	0·004				1·44	1·08, 1·92	0·012	1·50	1·12, 2·01	0·007	1·48	1·07, 2·05	0·017			
Q4	1·24	1·10, 1·40	0·004	1·40	1·24, 1·58	<0·001	1·38	1·19, 1·60	<0·001				1·38	1·04, 1·83	0·025	1·50	1·12, 2·00	0·007	1·61	1·12, 2·31	0·010			
$P_{\text{for trend}}$	0·002			<0·001			<0·001						0·024			0·005			0·008					

*Model 1: no covariates were adjusted.
†Model 2: adjusted for gender; age; race.
‡Model 3: adjusted for gender; age; race; poverty:income ratio; education level; insurance; marital status; alcohol intake per week; physical activity; comorbidity index; energy (kcal); BMI; smoking.
§DII quartile ranges: Quartile 1 = −5·18 to −0·12; Quartile 2 = −0·12 to 1·50; Quartile 3 = 1·50 to 2·88, Quartile 4 = 2·88 to 5·48

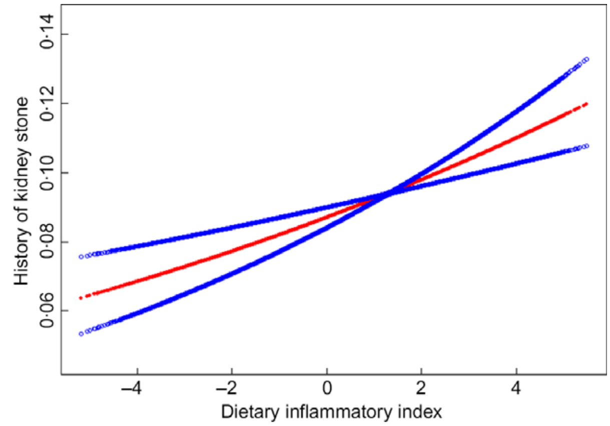

Fig. 1 (colour online) The non-linear relationship between Dietary Inflammatory Index and history of kidney stone

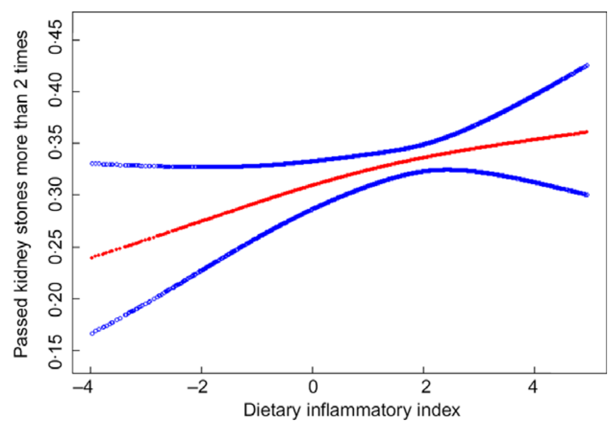

Fig. 2 (colour online) The non-linear relationship between Dietary Inflammatory Index and recurrent kidney stone

Discussion

We performed a correlation study in a large population of American adults, using a food-based pro-inflammatory dietary index to elucidate the relationship between potential inflammation of diet and kidney stones. The study demonstrates two important findings. First, the consumption of diets with greater inflammatory properties was significantly associated with a higher prevalence of kidney stones after adjusting for a variety of potential confounders. Higher dietary inflammation, as assessed by a high DII score, was correlated with a higher risk of developing kidney stones in men and women. Second, the risk of kidney stones recurrence rose as high as 61 % with the increase in dietary inflammation (Q4 *v.* Q1).

The incidence rates of kidney stones have been rising in many countries in recent years[1]. Besides, increased stone recurrence rates coupled with expensive treatments place a considerable burden on healthcare systems[2]. The previous studies showed that both genetic and environmental factors had contributions to the pathogenesis of the various types of stones synergistically[21]. Among environmental

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Table 3 Stratified logistic regression analysis to identify variables that modify the correlation between DII and kidney stones*,†

	Passed a kidney stone							Passed a kidney stone 2 times						
	n		Crude		Model II‡			*n*		Crude		Model II‡		
Subgroup	Crude	Model II‡	OR	95 % CI	OR	95 % CI	*P* (interaction)	Crude	Model II‡	OR	95 % CI	OR	95 % CI	*P* (interaction)
Age (years)							0·165							0·052
<60	13 229	13 229	1·06	1·02, 1·10	1·09	1·04, 1·13		649	649	0·98	0·90, 1·06	1·08	1·01, 1·15	
≥60	12 755	12 755	1·03	1·00, 1·06	1·05	1·02, 1·09		1212	1212	0·99	0·90, 1·10	1·11	1·03, 1·20	
Gender							0·212							0·390
Male	12 641	12 641	1·07	1·04, 1·10	1·08	1·04, 1·12		1034	1034	1·08	1·01, 1·16	1·08	1·00, 1·18	
Female	13 343	13 343	1·06	1·02, 1·09	1·05	1·01, 1·09		827	827	1·02	0·94, 1·11	1·03	0·94, 1·14	
BMI (kg/m^2)							0·932							0·655
<25	7487	7487	1·05	1·00, 1·10	1·07	1·02, 1·12		365	365	1·07	0·95, 1·20	1·03	0·98, 1·09	
≥25	18 497	18 497	1·04	1·01, 1·06	1·07	1·04, 1·10		1496	1496	1·09	0·96, 1·24	1·06	0·98, 1·14	
Poverty:income ratio							0·828							0·731
<1·3	7808	7808	1·06	1·02, 1·11	1·08	1·03, 1·13		561	561	1·06	0·96, 1·16	1·08	0·97, 1·20	
≥1·3and <3·5	11 060	11 060	1·04	1·00, 1·07	1·06	1·02, 1·10		797	797	1·04	0·97, 1·13	1·07	0·98, 1·17	
≥3·5	7116	7116	1·05	1·01, 1·09	1·07	1·03, 1·12		503	503	1·02	0·92, 1·12	1·03	0·92, 1·14	
Race/Ethnicity (%)							0·147							0·654
Mexican American	3990	3990	1·05	0·99, 1·11	1·07	1·01, 1·14		232	232	0·91	0·78, 1·07	0·95	0·80, 1·12	
Non-Hispanic Black	5496	5496	1·02	0·96, 1·08	1·04	0·98, 1·11		234	234	1·05	0·90, 1·22	1·07	0·90, 1·25	
Non-Hispanic White	11 095	11 095	1·04	1·01, 1·07	1·05	1·02, 1·09		1085	1085	1·07	1·00, 1·14	1·07	1·00, 1·14	
Other Hispanic	2758	2758	1·08	1·02, 1·16	1·10	1·02, 1·17		197	197	1·02	0·88, 1·19	1·04	0·89, 1·22	
Other race/ethnicity	2645	2645	1·15	1·06, 1·25	1·16	1·07, 1·26		113	113	1·08	0·88, 1·33	1·09	0·89, 1·35	
Insurance							0·983							0·062
	5800	5800	0·99	0·94, 1·04	1·02	0·97, 1·08		355	355	1·05	0·94, 1·17	1·06	0·94, 1·20	
	20 184	20 184	1·06	1·04, 1·09	1·08	1·04, 1·11		1506	1506	1·04	0·98, 1·10	1·06	0·99, 1·14	
Education (%)							0·993							0·347
Less school	6298	6298	1·06	1·01, 1·11	1·04	1·01, 1·07		465	465	0·97	0·87, 1·07	0·99	0·88, 1·11	
High school or GED	5722	5722	1·03	0·99, 1·08	1·07	1·02, 1·12		445	445	1·07	0·96, 1·19	1·10	0·97, 1·24	
More than high school	13 964	13 964	1·04	1·01, 1·07	1·07	1·03, 1·10		951	951	1·07	0·99, 1·14	1·08	1·00, 1·17	
Marital Status (%)							0·971							0·655
Married or living with partner	9512	9512	1·05	1·02, 1·08	1·05	1·01, 1·09		1233	1233	1·06	1·00, 1·13	1·01	0·93, 1·11	
Single	9512	9512	1·07	1·03, 1·10	1·07	1·03, 1·10		628	628	1·07	0·99, 1·16	1·04	0·94, 1·16	
Alcohol intake per week (%)							0·404							0·732
Never	4480	4480	1·05	1·00, 1·10	1·08	1·03, 1·14		438	438	1·06	0·95, 1·18	1·10	0·97, 1·23	
Up to once a week	16 411	16 411	1·04	1·01, 1·07	1·07	1·03, 1·10		1117	1117	1·02	0·96, 1·09	1·05	0·97, 1·14	
2–3 times a week	2771	2771	1·05	0·97, 1·14	1·09	1·01, 1·18		139	139	0·97	0·81, 1·15	0·98	0·81, 1·17	
4–6 times a week	1326	1326	0·94	0·85, 1·03	0·98	0·89, 1·08		95	95	1·10	0·87, 1·38	1·13	0·89, 1·43	
Daily or more	996	996	0·99	0·89, 1·10	1·03	0·92, 1·16		72	72	1·20	0·89, 1·61	1·19	0·88, 1·60	
Energy (kcal)							0·690							0·079
Low	12 982	12 982	1·06	1·02, 1·09	1·07	1·03, 1·11		943	943	1·01	0·92, 1·10	1·02	0·93, 1·11	
High	13 002	13 002	1·06	1·02, 1·09	1·06	1·02, 1·09		918	918	1·15	1·07, 1·25	1·13	1·04, 1·22	
Physical Activity (MET-based rank) (%)							0·168							0·038
Less than moderate	13 709	13 709	1·02	0·99, 1·05	1·05	1·01, 1·08		1122	1122	1·08	1·01, 1·16	1·10	1·01, 1·20	
Moderate	2475	2475	1·05	0·97, 1·14	1·10	1·01, 1·19		145	145	1·19	0·97, 1·46	1·25	1·01, 1·55	
Vigorous	9800	9800	1·06	1·02, 1·09	1·09	1·05, 1·14		594	594	0·97	0·90, 1·06	0·98	0·90, 1·08	

Table 3 *Continued*

Subgroup	Passed a kidney stone: *n* Crude	*n* Model II‡	Crude OR	Crude 95 % CI	Model II‡ OR	Model II‡ 95 % CI	*P* (interaction)	Passed a kidney stone 2 times: *n* Crude	*n* Model II‡	Crude OR	Crude 95 % CI	Model II‡ OR	Model II‡ 95 % CI	*P* (interaction)
Current or past cigarette smoker (%)							0·678							0·055
None	14 385	14 385	1·05	1·02, 1·09	1·07	1·04, 1·11		917	917	0·99	0·92, 1·06	1·01	0·93, 1·10	
Past	7236	7236	1·04	1·00, 1·07	1·05	1·01, 1·10		623	623	1·13	1·04, 1·23	1·16	1·05, 1·27	
Current	4363	4363	1·05	1·00, 1·11	1·08	1·02, 1·15		321	321	0·99	0·87, 1·13	1·01	0·87, 1·16	
Co-morbidity index (%)							0·813							0·226
0	14 895	14 895	1·04	1·00, 1·07	1·07	1·03, 1·11		756	756	1·00	0·92, 1·08	1·02	0·93, 1·11	
1, 2	10 406	10 406	1·03	1·00, 1·06	1·06	1·03, 1·10		1008	1008	1·08	1·01, 1·16	1·11	1·02, 1·21	
3, 4	683	683	1·05	0·95, 1·16	1·10	0·99, 1·22		97	97	0·96	0·79, 1·17	1·00	0·81, 1·22	

DII, Dietary Inflammatory Index.
*Independent variable: DII.
†Adjusted for gender; age; race; poverty:income ratio; education level; insurance; marital status; alcohol intake per week; physical activity; co-morbidity index; energy (kcal); BMI; smoking.
‡In each stratification, the model is not adjusted for the stratification variable.

factors, dietary habits are associated with a marked influence on the pathogenesis of nephrolithiasis and are likely contributing to the growing prevalence in the last few decades. Meschi *et al.*[22] suggested that citrus fruits contributed to increase urinary excretion of citrate and decrease calcium oxalate and urate saturation, which could effectively prevent kidney stones. Then, some micronutrients like Zn and Mg were found related to kidney stones, higher dietary Zn consumption may be correlated with an increased risk of kidney stone incidence[23], whereas increasing Mg consumption may be correlated with a lower risk of kidney stones[24]. Subsequently, in line with our study, Benjamin *et al.*[6] highlighted two important results that vegetarians had a lower risk of being hospitalised for kidney stones compared with those meat eaters. Then, among meat eaters, higher meat intake is correlated with an increased risk of developing kidney stones; on the other hand, increased consumption of high-fibre and fruit diets, and Mg-containing foods (bananas and almonds) may protect against the risk of stone occurrence.

Inflammation is an important biological pathway regulating the interaction between organisms and the environment, and diet intake is a major part of the environment[13]. Various foods are considered to be pro-inflammatory foods, like high sugar foods, refined grains, red and processed meats and fried foods, which can increase levels of inflammation[25]. In contrast, higher consumption of anti-inflammatory foods, such as legumes, unrefined cereals, nuts, fruits and vegetables[26], has been found to play the opposite role. The possible mechanism through which pro-inflammatory diets may weaken the hosts' immune defences include increased levels of CRP and IL-6[13], leucocytes as well as neutrophils[20], endoplasmic reticulum-stress reactivities provoked by SFA[27] and skewing of the redox balance[28].

In particular, several studies have shown that a higher DII score derived from a single 24 h is correlated with increased CRP in the US NHANES[29,30]. Nevertheless, there is relatively little knowledge about the effect of the inflammatory diet and immune system in kidney stone development. Shoag *et al.*[31] demonstrated a significantly positive correlation between CRP and kidney stone disease in younger patients. Then, they explained that the immune system and inflammatory pathways might play a significant role in the pathogenesis of nephrolithiasis in this age group, while this may not be applied to older people with renal stones.

In subgroup analysis, we revealed a relationship that the association between DII and recurrent nephrolithiasis in individuals with less than moderate and moderate physical activity was stronger than those with vigorous physical activity. It has been found that a regular exercise schedule could generate an overall reduction in inflammation at rest due to the anti-inflammatory environment produced by each exercise session combined with a reduction in visceral fat, which releases pro-inflammatory adipokines like TNF and IL-6[32]. Moreover, Sorensen *et al.*[33] conducted a

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cohort study including 84 225 post-menopausal women in 2014; they found that participants with a level of physical activity over 10 metabolic equivalent/week decreased a significant 30 % risk of developing nephrolithiasis after multivariate adjustment. Our research showed that there is no association between DII and kidney stones in participants with vigorous physical activity, but a significant positive correlation has been found in the other two groups, which indicates that increased exercise may decline the positive relationship between DII and kidney stones. In other words, people with a high pro-inflammatory diet intake could reduce the risk of recurrent nephrolithiasis through more exercise.

To the best of our knowledge, our study is the first to use the food-based DII score to link the relationship between diet-related inflammation and risk of kidney stones. We used a large well-defined cohort with appropriate weighting of survey participants, thereby allowing wide spread application of the findings to the US population. However, a single 24-h dietary recall may not take into account within-person variations in dietary intakes and is imprecise for characterising an individual's long-term intake habit, which means the kidney stone occurrence could have occurred years before the diet assessment[34]. Moreover, since the data in our study derived from a cross-sectional survey, the temporality of DII and kidney stones was unclear. Albeit the associations are of biological plausibility, the findings should be interpreted with caution and confirmatory longitudinal studies or clinical trials are warranted. Then, we cannot completely exclude the residual confounding by unmeasured or unknown variables, although we have adjusted for several potential confounders. Additionally, differentiating individuals based on stone composition or metabolic phenotypes might further illuminate the relationship with DII and present different aetiologies and pathogeneses.

Conclusion

Our findings revealed that a pro-inflammatory diet with a higher DII score is correlated with increased odds of kidney stones incidence and recurrence. These results might be meaningful to advise the public health community about this possible dietary approach to prevention kidney stone formation and recurrence, but a further study should be designed.

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Supplementary material

For supplementary material accompanying this paper visit https://doi.org/10.1017/S1368980021000793

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