Heliyon 9 (2023) e22930

Contents lists available at ScienceDirect

Heliyon

journal homepage: www.cell.com/heliyon

Association between the dietary inflammatory index and gout in the National Health and Nutrition Examination Survey 2007–2018

Yujun Zhang [a,b,1], Jingjing Song [a,b,1], Yizhong Lai [b], Ao Li [c], Yiwei Zhang [c], Haonan Zhou [c], Wentao Zhao [d], Zhen Zong [e], Rui Wu [a,*], Hui Li [a,**]

[a] Department of Rheumatology and Immunology, The First Affiliated Hospital of Nanchang University, 330006, Nanchang, China
[b] Nanchang University, 330006, Nanchang, China
[c] Queen Mary School, Nanchang University, 330006, Nanchang, China
[d] The 3rd Clinical Department of China Medical University, 10159, Shenyang, China
[e] Department of Gastrointestinal Surgery, The Second Affiliated Hospital of Nanchang University, 1 MinDe Road, 330006, Nanchang, China

ARTICLE INFO

Keywords:
NHANES
Dietary inflammatory index
Gout
Inflammation
Cross-sectional study

ABSTRACT

Objective: The aim of our study was to investigate whether the Dietary Inflammatory Index (DII) correlated with gout in American adults.
Method: The study used data from the 2007–2018 National Health and Nutrition Examination Survey, with 27,710 adults participating. Initially, multivariable analysis was performed, with controls for covariates, to assess the link of DII and gout. Then, restricted cubic splines (RCS) were applied to model the nonlinear relationship of DII and gout. Furthermore, propensity score matching (PSM) as a further study of potential relationships was established. Eventually, subgroup analysis was performed.
Result: Participants within the highest DII quartile would be more susceptible to increased risk of gout in the univariate regression model (Q4 vs. Q1, OR = 1.31, CI: 1.05–1.63). Additionally, a positive correlation was detected between gout risk and DII after adjusting on drinking, smoking, gender, race, age, and BMI. Based on RCS analysis, we observed that the risk of gout raised sharply as DII values increased, then flattened, and increased sharply again when the DII was greater than approximately 2.5. After performing the PSM, it was observed that DII correlated in a positive way to the presence of gout on a fully adjusted multivariable model. Subgroup analysis revealed that the link of DII and gout showed no statistical significance in females, blacks, Mexicans, nor in the population that smoked.
Conclusion: Greater degrees of pro-inflammation correlate with a higher risk of gout and might be a predisposing factor for gout. Hence, tactics fostering an anti-inflammatory diet for preventing and improving gout in adults should be regarded.

1. Introduction

Gout is the most common form of inflammatory arthritis and is related to impaired purine metabolism and excretion [1]. The

* Corresponding author.
** Corresponding author.
E-mail addresses: ndyfy00400@ncu.edu.cn (R. Wu), ndyfy04408@ncu.edu.cn (H. Li).
[1] These authors contributed equally to this work.

https://doi.org/10.1016/j.heliyon.2023.e22930
Received 30 April 2023; Received in revised form 19 November 2023; Accepted 22 November 2023
Available online 27 November 2023

sustained increase of serum uric acid leads to the precipitation of monosodium urate crystals within joints and other tissues, resulting in recurrent acute joint inflammation, uric acid nephropathy, and so on [2]. It has been reported that gout becomes increasingly prevalent across the world, with an incidence of approximately 3 cases per 1000 individuals annually [3]. Gout episodes are usually coupled with excruciating joint pain [4]. In addition, it has been validated that gout is associated with multiple comorbidities, such as obesity, hypertension, chronic kidney disease, erectile dysfunction, and other conditions [5]. Therefore, gout has largely impaired the life quality of patients and brings a heavy burden on the expenditure of medical care.

Various factors can contribute to the risk of gout, including age, genetic background, obesity, and comorbidities [6]. Moreover, the relationship between inflammation and the pathogenesis of gout has been well-determined in the past few decades [7,8]. Mechanically, macrophages ingest monosodium urate (MSU) crystals and induce the activation of NOD-like receptor thermal protein domain associated protein 3 (NLRP3) [9], which drives the pro-IL-1β to be cleaved to active IL-1β, leading to excruciating pain, joint swelling, and acute gouty inflammation [10]. Diets have a remarkable influence upon innate immune system phenotypes, and the chronic low-grade inflammatory levels derived from diets can exacerbate gouty inflammation [11]. Pro-inflammatory diets can induce the rise of inflammatory levels by eliciting macrophages to release chemokines and cytokines [12]. For instance, Western dietary patterns could switch the immune system into a pro-inflammatory phenotype [13], which aggravates gouty inflammation. Furthermore, long-time adherence to Western diets has been verified to increase the risk of gout [14]. On the contrary, anti-inflammatory diet patterns such as DASH diets, Mediterranean diets, or fiber- and vegetable-rich diets are associated with a low level of inflammation [14,15]. These dietary patterns can lower levels of serum uric acid and attenuate people's risk to gout or hyperuricemia by promoting a lower inflammatory response [16]. In addition, ketogenic diets, characterized by low carbohydrate, moderate protein, and high fat, have also been validated to ameliorate gouty inflammation. Ketogenic diets can elevate BHB, which impedes NLRP3/caspase-1-dependent IL-1βexpression in macrophages, thereby diminishing inflammatory responses [16]. Regarding the close relationship between dietary inflammation and gout, assessing the dietary inflammation potential are helpful for ameliorating and preventing gout.

The Dietary Inflammation Index (DII), a literature-derived dietary tool, was developed by Shivappa et al., in 2009 and updated in 2014 [17]. It offers a quantitative means to evaluate the overall inflammatory level of diets based on the balance of pro- and anti-inflammatory properties of its ingredients. DII of many inflammatory serum biomarkers such as *C*-reactive protein (CRP),

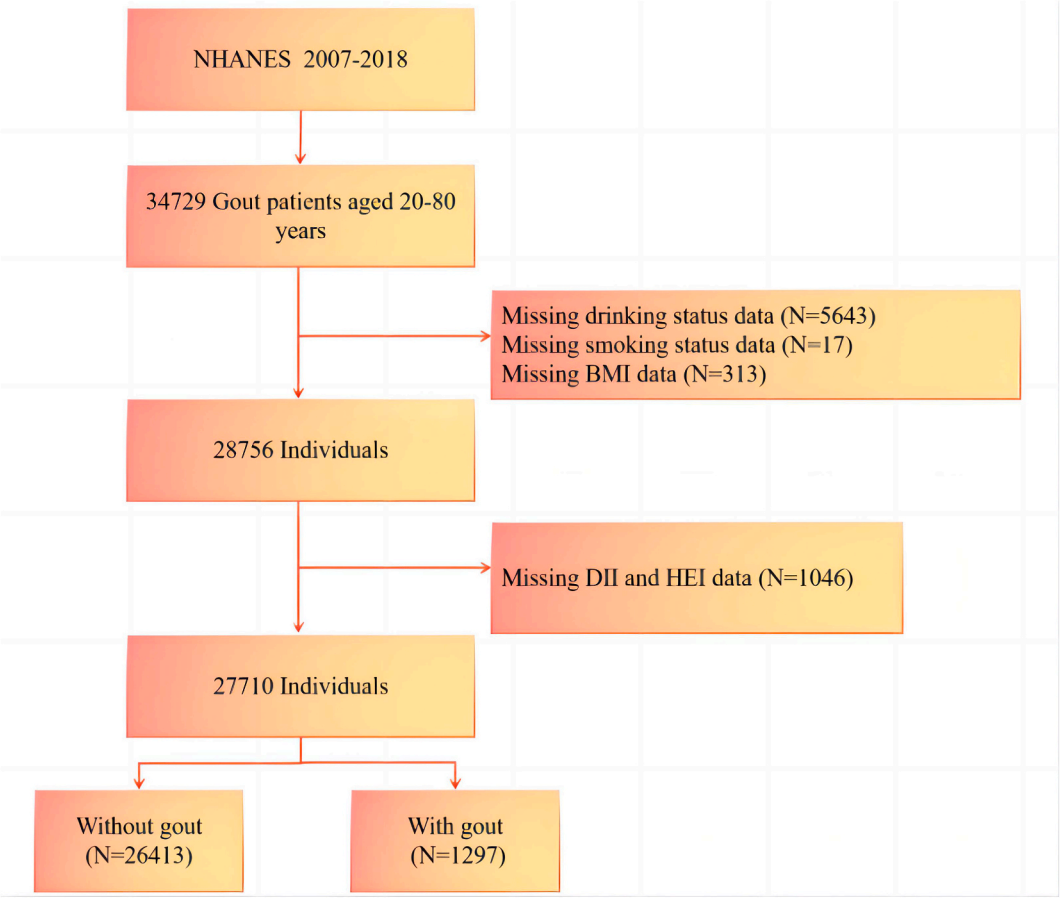

Fig. 1. Flowchart of the study population.

interleukin (IL)-6, IL-1β, IL-10, and tumor necrosis factor (TNF)-α has been validated in different ethnic groups [18–20]. Hitherto, there are large amounts of investigations that have assessed the relationship between DII and health problems, such as metabolic diseases, cardiovascular diseases, and erectile dysfunction [21–23]. Nevertheless, according to our knowledge, the relationship between dietary inflammation levels and gout has not been studied before. Hence, dependent on the National Health and Nutrition Examination Survey (NHANES) data, we conducted a cross-sectional study to decipher the correlation between DII and gout risk.

2. Materials and methods

2.1. Participants and study design

Our study analyzed the data collected from the NHANES. NHANES is administrated by the National Center for Health Statistics (NCHS). It is an open database intended to characterize the general condition of the American population in terms of health and nutrition. The database implements a graded, multi-stage probabilistic cluster sampling design for sorting out the characteristic participants in the survey. Before enrollment, all participants were provided with documented informed consent. Approval for this study was obtained from the Institutional Review Board of the Centers for Disease Control and Prevention. In the present study, six consecutive survey cycles of NHANES were selected (i.e., 2007–2008, 2009–2010, 2011–2012, 2013–2014, 2015–2016, 2016–2017, 2017–2018). The exclusion criteria were shown below: (1) participants with missing alcohol consumption data, (2) participants with missing smoking data, (3) participants with missing BMI data, and (4) participants with missing DII and Healthy Eating Index (HEI) data. In total, there were 27,710 individuals included in this study. Additional information on the study set-up was shown in Fig. 1.

2.2. Dietary information

The Nutrition Methods Working Group collected dietary information from all participants through a 24-h recalled diet interview conducted at the mobile examination center. Following the DII calculation proposed by Shivappa et al. [17], the DII score was determined according to the dietary effect on several inflammatory biomarkers (i.e. Il-1β, IL-4, IL-6, IL-10, TNF-α, and CPR). A "+1" score was assigned to a dietary component if it elevates the level of TNF-α, IL-6, IL-1β, and CRP or reduces the level of IL-10 and IL-4; by contrast, a "-1" score was assigned; if the level of inflammation biomarkers remains constant, then the dietary component was assigned "0" score. Entire diet factors were combined for the general DII score. Based on DII, the inflammatory potential of diets was regarded as pro-inflammatory (>0), anti-inflammatory (<0), or neither ($=0$). Firstly, the DII was analyzed as a continuous variant. Next, the participants were equally separated into four groups based on DII scores, recorded as Q4 (Q4 high DII), Q3 (higher middle DII), Q2 (lower middle DII), and Q1 (low DII). Additionally, we calculated the Healthy Eating Index (HEI) in the present study to determine diet quality. The HEI is a measurement applied in evaluating the consistency of a set of foods to the Dietary Guidelines for Americans (DGA). Higher HEI-2015 scores indicate higher quality of participants' diet. The HEI was also divided into quartiles (Q1 to Q4).

2.3. Definition of gout

On the health questionnaire, participants were asked "Have you ever been informed by a doctor or other health professional that you suffered from gout", and based on their answers, they were classified into the no-gout group and the gout group based on their answers.

2.4. Covariates

Socio-demographic and lifestyle information was obtained through standardized questionnaires. Baseline variables in this study included age (years), gender, race/ethnicity, BMI kg/m^2), alcohol consumption, and smoking. All detailed measurement procedures for the variables in this study could be found on the official NHANES website (www.cdc.gov/nchs/nhanes/(accessed January 16, 2023). Race/ethnicity was categorized as five clusters: non-Hispanic white, non-Hispanic black, Mexican American, and others. BMI contains four grades: BMI $\geq$30 kg/m^2 is obesity, 25–29.9 kg/m^2 is overweight, 18.5–24.9 kg/m^2 is normal weight, and $<$18.5 kg/m^2 is considered thin. Individuals who self-reported former or never smoking were defined as non-smokers. Non-drinkers were those who self-reported never drinking or having drunk in the past.

2.5. Statistical analysis

Categorical variables are shown as the number of participants (weighted percentages), and continuous variables are shown as weighted means (SDs). Adopting chi-square tests, Mann-Whitney U tests, and independent t-tests, we investigated baseline traits between those with and without gout. The "Spearman" approach for studying the relationship between DII and HEI was used. Subsequently, multivariate logistic regression was applied to explore the independent relationship between DII levels and gout. We made no factor adjustments to model 1. We made adjustments to race, drinking status, smoking status, and sex in model 2. Age and BMI were additionally adjusted in Model 3. To test whether there is a non-linear relationship that exists between DII and gout, a restricted cubic spline was performed. In addition, PSM employs the 1:3 nearest neighbor matching algorithm for matching participants with and without gout. Confounding factors such as age, gender, race, smoking status, drinking status, and BMI, were chosen for matching. Following PSM analysis, stratified analysis as a test of whether the association between DII and gout risk varied depending on gender,

age, race, smoking status, and alcohol consumption status was used. A two-sided p-value <0.05 was defined as having statistical significance. All statistical analyses were performed using R language 4.2.2 software.

3. Results

3.1. Characteristics of included subjects

There were totally 27,710 subjects taken into the definitive analysis, 1297 participants with gout and 26,413 participants without gout. The weighted number of all participants was 7,710,358, and the weighted prevalence of gout was 3.98 % (95 % CI 3.60%–4.36 %). In these two groups, age, sex, race, drinking, smoking, BMI, and DII were significantly different ($P < 0.05$). Participants having gout tended with older age and higher BMI. The prevalence of gout was less prevalent in males than females. (2.39 %, 95 % CI 2.03%–2.75 % vs. 5.65 %, 95 % CI 5.13%–6.16 %). Moreover, compared with those free of gout, the majority of subjects with gout drank alcohol, whereas the minority smoked. Furthermore, regarding indexes that assess inflammation levels and the quality of the diet of participants, gout-free participants had lower DII levels (mean DII, 1.39 vs 1.57). Nonetheless, no significant difference in HEI scores ($P = 0.86$) was found between the gout and non-gout groups. Additionally, we explored the relationship between HEI and DII in the same population and recovered a notably negative relationship ($R = -0.48$; $p < 0.001$) (Fig. 2). Considering that gout is an inflammatory disease and DII focuses more on inflammation, we speculated that DII might be a better indicator of gout.

3.2. Association between DII and gout

3.2.1. Multiple regression model

Table 2 exhibits the results of sample-weighted logistic regression analyses. The correlation between DII and gout was reliable in various adapted models. In the unadjusted model (model 1), subjects within the highest DII quartiles were at a higher risk of gout versus those within the lowest DII quartiles [OR 1.31 (95 % CI, 1.05–1.63)]. Moreover, across the main model (model 2) corrected for sex, smoking status, and drinking status, the OR were 1.49 (95 % CI, 1.17–1.90) and 1.67 (95 % CI, 1.32–2.12) for DII quartiles 3 and 4, respectively (p for trend = <0.001). Furthermore, the correlation remained constant and the tendency was pronounced in the fully corrected model (model 3) (P for trend = 0.012).

3.2.2. Non-linear association research between DII and gout

The possibility of a non-linear relationship between DII and gout was further investigated using a four-knot restricted cubic spline. The p-value of 0.12 for the non-linearity test indicates that no significant non-linear correlation exists between DII and gout after controlling for all covariates. Fig. 3 illustrates the overall upward inclination of the curve, which shows a substantial positive connection between gout and DII. According to the curve, when the diet is in anti-inflammatory mode (DII<0), the OR is lower than 1, which means that an anti-inflammatory diet reduces the risk of gout. Subsequently, OR tends to 1 until DII reaches about 2.5. Afterward, the OR value increases dramatically.

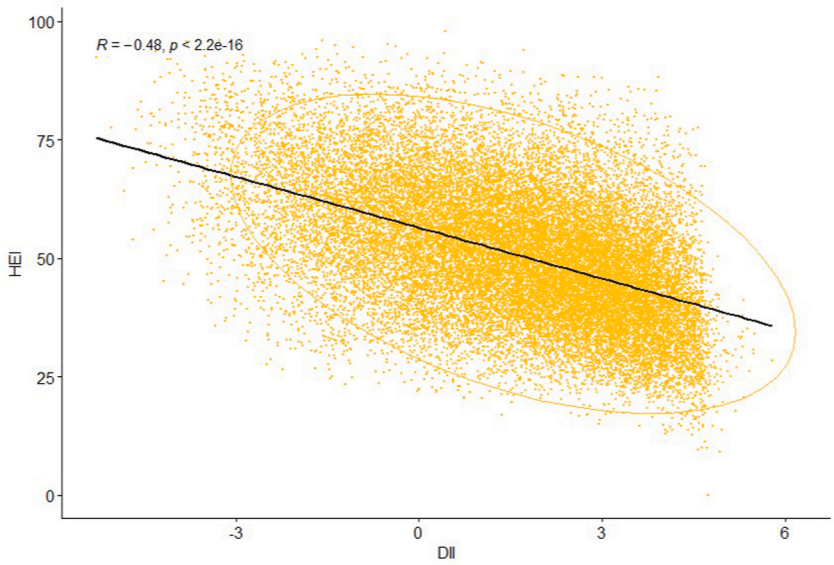

Fig. 2. Association between the HEI and DII.

Table 1
Weighted distributions of characteristics of participants[a].

Characteristic	Gout		P value
	No, N = 26,413	Yes, N = 1297	
Age	46.74 (0.25)	60.68 (0.52)	**<0.001**
Sex			**<0.001**
Male	12,723 (47.94)	916 (69.23)	
Female	13,690 (52.06)	381 (30.77)	
Ethnicity			**<0.001**
Non-Hispanic white	11,072 (67.46)	644 (74.21)	
Non-Hispanic black	5539 (10.86)	346 (12.58)	
Mexican American	4085 (8.56)	98 (3.74)	
Other races	5717 (13.12)	209 (9.47)	
Drinking			**<0.001**
No	7870 (23.30)	467 (30.32)	
Yes	18,543 (76.70)	830 (69.68)	
Smoking			**0.015**
No	20,968 (80.37)	1079 (85.07)	
Yes	5445 (19.63)	218 (14.93)	
Body Mass Index			**<0.001**
Normal weight	7204 (28.33)	188 (12.86)	
Overweight	8722 (32.90)	396 (30.23)	
Obesity	10,075 (37.26)	702 (56.42)	
Thin	412 (1.51)	11 (0.48)	
HEI	50.84 (0.22)	50.75 (0.53)	0.86
DII	1.39 (0.03)	1.57 (0.07)	**0.012**

[a] Categorical variables are shown as the number of participants (weighted percentages), and continuous variables are shown as weighted means (SDs). DII, Dietary Inflammatory Index; HEI, healthy eating index.

Table 2
Association of DII with gout[a].

DII	Model 1	P value	Model 2	P value	Model 3	P value
Q1	reference		reference		reference	
Q2	1.34 (1.05,1.70)	**0.02**	1.44 (1.13,1.84)	**0.004**	1.41 (1.10,1.81)	**0.01**
Q3	1.26 (1.00,1.60)	0.05	1.49 (1.17,1.90)	**0.001**	1.37 (1.05,1.80)	**0.02**
Q4	1.31 (1.05,1.63)	**0.02**	1.67 (1.32,2.12)	**<0.001**	1.47 (1.12,1.93)	**0.01**
P for trend	**0.043**		**<0.001**		**0.012**	

[a] Data are presented as odds ratio (OR) [95 % confidence interval (CI)]. DII, Dietary Inflammatory Index; Q1, low DII; Q2, medium-low DII; Q3, medium-high DII; Q4, high DII. Model 1: crude model. Model 2: adjusted for sex, race, smoking status, and drinking status. Model 3: as model 2 and additionally adjusted for age and BMI.

3.2.3. PSM analysis

To further study the relationship between DII and gout risk, we used the nearest neighbor PSM approach (1:3) to create a control group that was comparable to the gout group. After balancing variations in age, gender, race, smoking status, drinking status, and BMI, we included 3891 participants in the non-gout group and 1297 participants in the gout group. Subsequent analysis results (Table 3) showed that all baseline traits among the two groups were not statistically significant. Coherently to the pre-match findings, DII remained statistical significance ($p = 0.001$) across groups following matching. After re-analyzing using multifactorial logistic regression analysis, it was revealed that gout risk increased with rising DII (Table 4). Moreover, a strong linear association with gout risk was observed for all levels of DII in all models.

To investigate the influence of dietary factors on DII between gout and non-gout patients, scores for each dietary component were also presented in Table 3. It was exhibited that higher inflammatory scores for dietary fiber, vitamin A, β-carotene, vitamin B2, niacin, folate, vitamin C, vitamin D, magnesium, and zinc in gout patients, while lower inflammatory scores were found for carbohydrate, total saturated fatty acid, vitamin B12, and iron.

3.2.4. *Subgroup analyses after PSM*

Subsequently, the stratified analysis was conducted to evaluate whether the correlation between DII and gout risk varied by gender, age (<60 and ≥ 60 years), race, smoking status, and drinking status. When the stratified analysis was performed by gender, the correlation between DII and gout risk showed significant only in male individuals (Fig. 4). Among males, the medium-low (Q2), medium-high (Q3), and highest quartiles (Q4) of the DII were correlated with a higher risk of gout. Interestingly, the correlation of the Q2, Q3, and Q4 of DII with increased risk of gout also existed in whites and the non-smoking group. However, in other races and the smoking group, DII and gout risk were not significantly associated. Moreover, in stratified subgroup analysis according to drinking status, a stronger positive association between the Q4 of DII and gout risk was found in the non-drinking group (Q4 vs Q1: OR = 2.06;

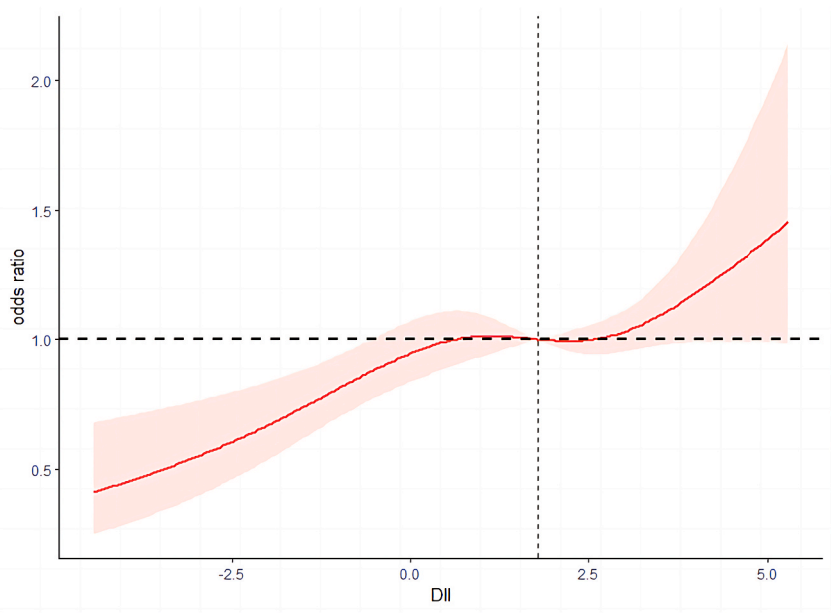

Fig. 3. Association between DII and gout: a RCS analysis.

95 % CI, 1.35–3.14) but not the drinking group (Q4 vs Q1: OR = 1.31; 95 % CI, 0.90–1.91) after completely modeling adjustment. The linear correlation between DII and gout risk was also only present in the non-drinking group (P for trend = 0.08,0.003, respectively). However, the linear correlation between the Q4 of DII and gout risk was present in both individuals aged <60 years old groups and individuals aged ≥60 years old groups (P for trend = 0.01,0.04, respectively). The test for interaction demonstrated the effect of DII on gout was significantly influenced by alcohol consumption (P for interaction <0.05), whereas no significant interactions were observed between other groups (all P for interactions >0.05).

4. Discussion

Among this large-scale cross-sectional study, it was estimated the 12-year prevalence of gout in the United States is approximately 3.98 % (95 % CI 3.60%–4.36 %). Interestingly, the gout incidence in females is lower than in males (2.39%vs.5.65 %) [24], which is possibly due to estrogen-stimulated uric acid excretion [4]. In addition, a significant positive relationship was detected for DII and gout incidence, suggesting that inflammation-promoting diets may related to an increased risk of gout. Given that inflammation is closely correlated to the pathogenesis of gout and the correlation between HEI and gout risk is not significant, we speculate that DII may be a better indicator of gout than HEI. The results from multivariable logistic regression analyses suggest that DII is positively associated with gout, and this association remains stable in different adjusted models. Restricted cubic splines visualize the relationship between gout and DII. It was exhibited that the risk of gout became remarkably higher when the DII surpassed about 2.5. Accordingly, there is a great need to adjust the DII value within a certain range. In the 1:3 PSM reanalysis, all levels of DII were positively associated with gout risk in all models. PSM reanalysis further confirmed the validity of the results. Subgroup analysis showed a positive association between DII and gout risk that varied across populations. It reveals that gender, age, race, smoking status, and alcohol consumption status are confounding factors that disturb the relationship between DII and gout risk.

Unhealthy dietary habits have been recognized as an important source of low-grade chronic inflammation, which may aggravate gouty inflammation [25]. Therefore, the dietary pattern may associate with gout, which can be associated via the impacts of inflammation. For example, the Western dietary pattern (rich in saturated fat, refined carbohydrate, and red meats) has been confirmed to correlate with a high level of serum inflammatory biomarkers [26,27]. A previous prospective cohort study initiatively investigated the association between Western diets and gout risk. Its landmark findings delineate that the Western diet score is positively correlated with gout risk [28]. In contrast, the Dietary Approaches to Stop Hypertension (DASH) diet (abundant with fruits, vegetables, and complete grains) has been shown to have anti-inflammatory effects as an effective antihypertensive diet plan [29]. A randomized feeding trial found that serum uric acid concentration is diminished after 30 days of DASH diet intervention [30], consistent with the results discovered by Juraschek et al. in both gout-free hypertensive patients and gout patients [31,32]. Furthermore, an inverse correlation was found between the risk of hyperuricemia as well as gout and the DASH score [33]. Similarly, the Mediterranean diet as an anti-inflammatory diet has been extensively studied for its protective effect against gout. According to findings from the IKARIA study, long-term adherence to the Mediterranean diet could effectively mitigate the prevalence of hyperuricemia [34]. Moreover, both observational and intervention studies have reported that the Mediterranean diet can reduce uric acid levels [35–37]. Thus, it can be deduced that dietary inflammation potential is closely associated with gout. In our research, the DII was adopted to evaluate the dietary inflammation potential. DII of the gout group was markedly above that of the gout-free group (Table 1).

Table 3
Weighted distributions of characteristics of participants after propensity score matching (PSM)[a].

Characteristics		Non-Gout (N = 3891)	Gout (N = 1297)	P value
Age		60.38 (0.34)	60.68 (0.52)	0.61
Sex				0.28
	Male	2751 (71.33 %)	916 (69.23 %)	
	Female	1140 (28.67 %)	381 (30.77 %)	
Ethnicity				0.25
	Non-Hispanic white	1974 (76.86 %)	644 (74.21 %)	
	Non-Hispanic black	985 (10.89 %)	346 (12.58 %)	
	Mexican American	316 (3.23 %)	98 (3.74 %)	
	Other races	616 (9.02 %)	209 (9.47 %)	
Drinking status				0.99
	No	1431 (30.30 %)	467 (30.32 %)	
	Yes	2460 (69.70 %)	830 (69.68 %)	
Smoking status				0.62
	No	3332 (85.95 %)	1079 (85.07 %)	
	Yes	559 (14.05 %)	218 (14.93 %)	
BMI				0.34
	Normal weight	527 (11.83 %)	188 (12.86 %)	
	Overweight	1188 (28.87 %)	396 (30.23 %)	
	Obesity	2164 (59.09 %)	702 (56.42 %)	
	Thin	12 (0.22 %)	11 (0.48 %)	
DII		1.27 (0.05)	1.57 (0.07)	**0.001**
HEI		51.70 (0.33)	50.75 (0.53)	0.14
Energy		0.00 (0.00)	−0.01 (0.01)	0.10
Protein		0.00 (0.00)	0.00 (0.00)	0.06
Carbohydrate		−0.02 (0.00)	−0.03 (0.00)	**0.02**
Dietary fiber		0.15 (0.01)	0.21 (0.02)	**0.02**
Total fatty acid		0.05 (0.01)	0.03 (0.01)	0.05
Total saturated fatty acid		−0.05 (0.01)	−0.08 (0.01)	**0.03**
MUFA		0.00 (0.00)	0.00 (0.00)	0.05
PUFA		−0.09 (0.01)	−0.07 (0.01)	0.33
Cholesterol		−0.01 (0.00)	−0.02 (0.00)	0.21
Vitamin A		0.17 (0.00)	0.20 (0.01)	**0.001**
β-Carotene		0.32 (0.01)	0.35 (0.01)	**0.02**
Vitamin B1		0.01 (0.00)	0.02 (0.00)	0.06
Vitamin B2		−0.02 (0.00)	−0.01 (0.00)	**<0.001**
Niacin		0.01 (0.00)	0.03 (0.01)	**0.03**
Vitamin B6		−0.11 (0.01)	−0.08 (0.01)	0.05
Folate		0.10 (0.00)	0.12 (0.01)	**0.02**
Vitamin B12		−0.01 (0.00)	−0.02 (0.00)	**<0.001**
Vitamin C		0.20 (0.01)	0.23 (0.01)	**0.02**
Vitamin D		0.19 (0.01)	0.24 (0.01)	**<0.001**
Vitamin E		0.08 (0.01)	0.10 (0.02)	0.20
Magnesium		0.02 (0.01)	0.06 (0.01)	**0.01**
Iron		0.00 (0.00)	0.00 (0.00)	**0.01**
Zinc		−0.05 (0.01)	0.01 (0.01)	**<0.001**
Selenium		−0.11 (0.00)	−0.10 (0.00)	0.10
Caffeine		0.08 (0.00)	0.08 (0.00)	0.40
Alcohol		0.15 (0.01)	0.14 (0.01)	0.40
n3 Polyunsaturated fatty acid		0.27 (0.00)	0.27 (0.00)	0.92
n6 Polyunsaturated fatty acid		−0.07 (0.00)	−0.06 (0.00)	0.23

[a] Categorical variables are shown as the number of participants (weighted percentages), and continuous variables are shown as weighted means (SDs). DII, Dietary Inflammatory Index; HEI, healthy eating index.

Table 4
Association of DII with gout after propensity score matching (PSM)[a].

DII	Model 1	P value	Model 2	P value	Model 3	P value
Q1	ref		ref		ref	
Q2	1.38 (1.05,1.83)	**0.02**	1.38 (1.04,1.83)	**0.03**	1.38 (1.04,1.83)	**0.03**
Q3	1.43 (1.09,1.88)	**0.01**	1.42 (1.08,1.88)	**0.01**	1.42 (1.07,1.88)	**0.02**
Q4	1.58 (1.21,2.07)	**0.001**	1.57 (1.18,2.09)	**0.002**	1.57 (1.18,2.09)	**0.003**
P for trend	**0.001**		**0.003**		**0.003**	

[a] Data are presented as odds ratio (OR) [95 % confidence interval (CI)]. DII, Dietary Inflammatory Index; Q1, low DII; Q2, medium-low DII; Q3, medium-high DII; Q4, high DII. Model 1: crude model. Model 2: adjusted for sex, race, smoking status, and drinking status. Model 3: as model 2 and additionally adjusted for age and BMI.

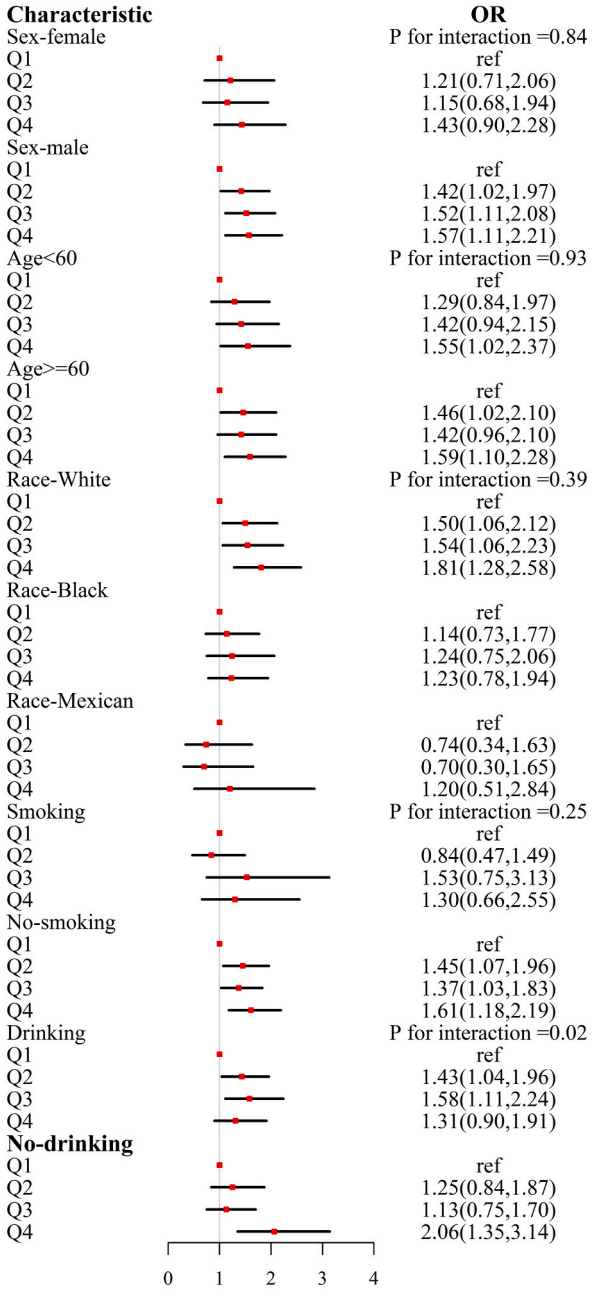

Fig. 4. Subgroup analyses for the association of DII with the risk of gout.

Moreover, the results from multivariable logistic regression analyses showed that DII was positively related to gout in all models (Table 2). The results of logistic regression analysis after adjusting for all confounders showed the gout risk of the population was 1.47 fold higher at the Q4 level of DII than in the Q1 level of DII (OR:1.47, 95 % CI, 1.12–1.93). This association remained even after the confounding factors were balanced by PSM (Table 4).

Furthermore, we used RCS to visualize the association between gout and DII (Fig. 3). Interestingly, according to the curve, the risk of gout did not increase until the DII reached about 2.5, indicating that a threshold for the effect of pro-inflammatory dietary patterns on gout might exist. A pro-inflammatory dietary pattern with a DII lower than 2.5 may not produce enough levels of inflammation to induce gout. In other words, when the diet was in anti-inflammatory mode, the risk of gout may be significantly reduced. Hence, those participants whose DII is higher than 2.5 need to be more cautious about their risk of gout.

The global burden of gout analysis 1990–2019 shows that controlling dietary factors and recognizing the increased burden of gout in obese patients can help reduce the burden of gout worldwide, including in areas with high sociodemographic index [38]. A

systematic review of dietary and nutritional contributors to the development of gout was presented by Zhang et al. They found that energy-type nutritional overloads diets such as high-sugar and high-fat diets can induce hyperuricemia and inflammation, whereas adequate intake of essential nutrients is highly beneficial in gout [11]. Vitamins like vitamin A [39], vitamin D [40], and vitamin C [41,42] exhibit helpful anti-oxidative stress and anti-inflammatory effects with effective reduction of serum uric acid levels. Increasing the consumption of vitamins, fiber as well as unsaturated fatty acids, and supplementing with the right amount of minerals together with premium protein, can improve gout symptoms by promoting systemic metabolism [28,43]. In the PSM analysis, we examined the differences in dietary components of DII among individuals. These findings indicate that gout patients have elevated inflammatory scores for dietary fiber, vitamin A, β-carotene, vitamin B2, niacin, folate, vitamin C, vitamin D, magnesium, and zinc, most of which are known to provide relief for gout (Table 3). It was speculated that the lower-than-average intake of these counter-inflammatory ingredients among gout sufferers leads to higher inflammation scores for these nutrients. The important zinc effect on the management of gout continues to be investigated by researchers. Research has indicated that zinc oxide nanoparticles are effective in reducing oxidative stress and treating gouty arthritis [44]. Furthermore, folate and zinc can improve hypo-uricemia through the regulation of the microbiome in the gut to repress uric acid synthesis and promote uric acid elimination [45]. It is suggested that moderate zinc intake may have a positive impact on the prognosis of patients with gout. By moderately increasing the intake of some counter-inflammatory ingredients including folate and zinc, gout sufferers can effectively reduce their inflammatory response, thus potentially preventing and treating gout [46–48].

In subgroup analysis, DII had various effects on people with distinct sex, age, ethnicity, smoking status, and drinking status, suggesting that more precise preventive strategies should be implemented for gout (Fig. 4). It showed that the correlation of DII with gout risk was more intense among males than among females. Among the males, the correlation of DII at all levels with gout was pronounced. The differences between the two groups might be attributed to risk genetic factors [49]. In a recent survey, Lin et al. investigated the impact of risk genetic factors of gout on the relationship between diet and gout risk [50]. The genetic risk score was structured by using previously identified single nucleotide polymorphisms (SNPs) [51]. Their findings discovered an increasing relation of diet to gout risk among participants with higher genetic risks [50]. Given that gout is more prevalent among the elderly compared to younger individuals, we examined the relationship between DII and gout across distinct age cohorts, with a demarcation point at 60 years of age [52]. Our findings revealed that elevated DII values in different age groups correlated markedly to greater gout risk. Traditionally, gout has been regarded as an affluent white-male disorder, and they tend to over-indulge of alcohol as well as other foods rich in purines [53]. Our study reveals that there is a significant increase in the risk of gout among white individuals as their DII levels rise (OR:1.81, 95 % CI, 1.28–2.58). However, this association was not observed among black and Mexican populations. Therefore, whites need to be mindful of their dietary habits and decrease their consumption of pro-inflammatory foods, which may prevent the onset of gout.

It is well-accepted that lifestyle habits including drinking and smoking are critical factors in determining the risk of gout. In the subgroup stratified by smoking status, our results did not show an association between DII and gout in the smoking group, but the association was strong in the non-smoking group. We speculate that this condition may be due to the fact that smoking reduces serum uric acid levels by interacting with superoxide metabolism, attenuating the influence of a pro-inflammatory diet on gout risk [54]. Moreover, alcohol is considered a risk factor for gout attacks in the Dietary Guidelines for Americans. Many authors now agree that even moderate alcohol consumption can trigger gout attacks, regardless of the type of alcohol [55]. However, a mendelian randomization study has shown no causal role for increased alcohol consumption in the development of gout [56]. Most importantly, our study found remarkable effects of alcohol consumption on DII in terms of the occurrence of gout. It was observed that in the non-drinking group, as DII levels increased, the risk of gout also increased significantly (Q4 vs. Q1, OR = 2.03, CI:1.25–3.14) and this trend was evident (P for trend = 0.003). However, in the drinking group, this trend was not observed (P for trend = 0.08). These differences in DII and gout risk between the drinking and non-drinking groups require further investigation.

The study we conducted offers a couple of strengths and insights. First, given this inclusion of a wide sample size, there is enough statistical power to give precise and reliable conclusions about this first study exploring the association between DII and gout. Second, our study adopts RCS analysis, which further supports that there is a linear relationship that exists among DII and gout, where the trend of the RCS curve and critical value might purvey new evidence for health policymakers. Furthermore, we demonstrated an association between DII and gout risk by multivariate logistic regression. PSM analysis confirmed the reliability and accuracy of this association. However, this study also has some limitations. Firstly, although the importance of an anti-inflammatory diet in preventing and improving gout is supported by previous studies [57,58], the cross-sectional nature of our study made it impossible to determine causality as in the Mendelian randomization study. Further studies, such as randomized controlled trials, need to be conducted to explore whether there is a causal relationship between dietary inflammation and gout. Secondly, although potential confounders were adjusted as much as possible, some residual or unmeasured confounders might still exist. Thirdly, the DII was computed based on the 24-h recalled diet interview included in this study, which may be biased. Last but not least, these conclusions come from a national survey in the United States, so they probably cannot be generalized to cover other racial groups.

5. Conclusions

As a conclusion, our findings indicate an association of a pro-inflammatory diet with increased gout risk among US adults, which provides clues for further large-scale prospective studies to explore the relationship between dietary inflammation and gout. These findings may help to design tailored dietary plans by controlling dietary inflammation levels for gout patients or individuals with a high risk of gout to alleviate or prevent gout.

Ethics approval and consent to participate

The protocols of NHANES were approved by the institutional review board of the National Center for Health Statistics, CDC (https://www.cdc.gov/nchs/nhanes/irba98.htm). NHANES has obtained written informed consent from all participants.

Availability of data and materials

The datasets generated and analyzed in the current study are available at NHANES website: https://www.cdc.gov/nchs/nhanes/index.htm.

Funding

This research was financially supported by "TCM scientific research project of Jiangxi Provincial Health and Family Planning Commission" (Grant Number: 2018B038) and "Research subject of educational reform of Nanchang University" (NCUJGLX-2022-160-96).

CRediT authorship contribution statement

Yujun Zhang: Data curation, Formal analysis. **Jingjing Song:** Data curation, Formal analysis. **Yizhong Lai:** Methodology. **Ao Li:** Validation. **Yiwei Zhang:** Writing – original draft. **Haonan Zhou:** Writing – review & editing. **Wentao Zhao:** Writing – review & editing. **Zhen Zong:** Formal analysis. **Rui Wu:** Conceptualization. **Hui Li:** Conceptualization.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:Hui Li reports financial support was provided by Science and Technology plan of Jiangxi Provincial Health and Family Planning Commission. Hui Li reports financial support was provided by TCM scientific research project of Jiangxi Provincial Health and Family Planning Commission. Hui Li reports financial support was provided by Research subject of educational reform of Nanchang University.

Acknowledgments

The authors thank the participants of the NHANES databases.

References

[1] N. Dalbeth, T.R. Merriman, L.K. Stamp, Gout, Lancet 388 (10055) (2016) 2039–2052.
[2] P. Richette, T. Bardin, Gout, Lancet 375 (9711) (2010) 318–328.
[3] M. Dehlin, L. Jacobsson, E. Roddy, Global epidemiology of gout: prevalence, incidence, treatment patterns and risk factors, Nat. Rev. Rheumatol. 16 (7) (2020) 380–390.
[4] N. Dalbeth, A.L. Gosling, A. Gaffo, A. Abhishek, Gout, Lancet 397 (10287) (2021) 1843–1855.
[5] Y. Zhu, B.J. Pandya, H.K. Choi, Comorbidities of gout and hyperuricemia in the US general population: NHANES 2007-2008, Am. J. Med. 125 (7) (2012) 679–687.e671.
[6] J.A. Singh, S.G. Reddy, J. Kundukulam, Risk factors for gout and prevention: a systematic review of the literature, Curr. Opin. Rheumatol. 23 (2) (2011) 192–202.
[7] A.K. So, F. Martinon, Inflammation in gout: mechanisms and therapeutic targets, Nat. Rev. Rheumatol. 13 (11) (2017) 639–647.
[8] Z. Lan, L. Chen, J. Feng, Z. Xie, Z. Liu, F. Wang, P. Liu, X. Yue, L. Du, Y. Zhao, et al., Mechanosensitive TRPV4 is required for crystal-induced inflammation, Ann. Rheum. Dis. 80 (12) (2021) 1604–1614.
[9] F. Martinon, V. Pétrilli, A. Mayor, A. Tardivel, J. Tschopp, Gout-associated uric acid crystals activate the NALP3 inflammasome, Nature 440 (7081) (2006) 237–241.
[10] J. Desai, S. Steiger, H.J. Anders, Molecular pathophysiology of gout, Trends Mol. Med. 23 (8) (2017) 756–768.
[11] Y. Zhang, S. Chen, M. Yuan, Y. Xu, H. Xu, Gout and diet: a comprehensive review of mechanisms and management, Nutrients 14 (17) (2022).
[12] Y. Bordon, Macrophages: shaping good eating habits, Nat. Rev. Immunol. 16 (12) (2016) 719.
[13] A.R. Saltiel, J.M. Olefsky, Inflammatory mechanisms linking obesity and metabolic disease, J. Clin. Invest. 127 (1) (2017) 1–4.
[14] C. Yokose, N. McCormick, N. Lu, A.D. Joshi, G. Curhan, H.K. Choi, Adherence to 2020 to 2025 dietary Guidelines for Americans and the risk of new-onset female gout, JAMA Intern. Med. 182 (3) (2022) 254–264.
[15] E.L. Goldberg, J.L. Asher, R.D. Molony, A.C. Shaw, C.J. Zeiss, C. Wang, L.A. Morozova-Roche, R.I. Herzog, A. Iwasaki, V.D. Dixit, β-Hydroxybutyrate deactivates neutrophil NLRP3 inflammasome to relieve gout flares, Cell Rep. 18 (9) (2017) 2077–2087.
[16] A.T. Vieira, I. Galvão, L.M. Macia, M. Sernaglia É, M.A. Vinolo, C.C. Garcia, L.P. Tavares, F.A. Amaral, L.P. Sousa, F.S. Martins, et al., Dietary fiber and the short-chain fatty acid acetate promote resolution of neutrophilic inflammation in a model of gout in mice, J. Leukoc. Biol. 101 (1) (2017) 275–284.
[17] N. Shivappa, S.E. Steck, T.G. Hurley, J.R. Hussey, J.R. Hébert, Designing and developing a literature-derived, population-based dietary inflammatory index, Publ. Health Nutr. 17 (8) (2014) 1689–1696.
[18] S. Vieujean, B. Caron, V. Haghnejad, J.Y. Jouzeau, P. Netter, A.C. Heba, N.C. Ndiaye, D. Moulin, G. Barreto, S. Danese, et al., Impact of the exposome on the epigenome in inflammatory bowel disease patients and animal models, Int. J. Mol. Sci. 23 (14) (2022).
[19] S.R. Millar, P. Navarro, J.M. Harrington, N. Shivappa, J.R. Hébert, I.J. Perry, C.M. Phillips, Dietary score associations with markers of chronic low-grade inflammation: a cross-sectional comparative analysis of a middle- to older-aged population, Eur. J. Nutr. 61 (7) (2022) 3377–3390.
[20] N. Shivappa, J.R. Hebert, A. Marcos, L.E. Diaz, S. Gomez, E. Nova, N. Michels, A. Arouca, E. González-Gil, G. Frederic, et al., Association between dietary inflammatory index and inflammatory markers in the HELENA study, Mol. Nutr. Food Res. 61 (6) (2017).

[21] Q. Zhao, X. Tan, Z. Su, H.P. Manzi, L. Su, Z. Tang, Y. Zhang, The relationship between the dietary inflammatory index (DII) and metabolic syndrome (MetS) in middle-aged and elderly individuals in the United States, Nutrients 15 (8) (2023).
[22] L. Wu, Y. Shi, C. Kong, J. Zhang, S. Chen, Dietary inflammatory index and its association with the prevalence of coronary heart disease among 45,306 US adults, Nutrients 14 (21) (2022).
[23] Z. Ruan, X. Xie, H. Yu, R. Liu, W. Jing, T. Lu, Association between dietary inflammation and erectile dysfunction among US adults: a cross-sectional analysis of the National Health and Nutrition Examination Survey 2001-2004, Front. Nutr. 9 (2022), 930272.
[24] N. McCormick, N. Lu, C. Yokose, A.D. Joshi, S. Sheehy, L. Rosenberg, E.T. Warner, N. Dalbeth, T.R. Merriman, K.G. Saag, et al., Racial and sex disparities in gout prevalence among US adults, JAMA Netw. Open 5 (8) (2022), e2226804.
[25] L. Galland, Diet and inflammation, Nutr. Clin. Pract. 25 (6) (2010) 634–640.
[26] A. Johansson-Persson, M. Ulmius, L. Cloetens, T. Karhu, K.H. Herzig, G. Onning, A high intake of dietary fiber influences C-reactive protein and fibrinogen, but not glucose and lipid metabolism, in mildly hypercholesterolemic subjects, Eur. J. Nutr. 53 (1) (2014) 39–48.
[27] D.E. King, B.M. Egan, M.E. Geesey, Relation of dietary fat and fiber to elevation of C-reactive protein, Am. J. Cardiol. 92 (11) (2003) 1335–1339.
[28] S.K. Rai, T.T. Fung, N. Lu, S.F. Keller, G.C. Curhan, H.K. Choi, The Dietary Approaches to Stop Hypertension (DASH) diet, Western diet, and risk of gout in men: prospective cohort study, BMJ 357 (2017) j1794.
[29] S. Soltani, F. Shirani, M.J. Chitsazi, A. Salehi-Abargouei, The effect of dietary approaches to stop hypertension (DASH) diet on weight and body composition in adults: a systematic review and meta-analysis of randomized controlled clinical trials, Obes. Rev. 17 (5) (2016) 442–454.
[30] S.P. Juraschek, A.C. Gelber, H.K. Choi, L.J. Appel, E.R. Miller 3rd, Effects of the dietary approaches to stop hypertension (DASH) diet and sodium intake on serum uric acid, Arthritis Rheumatol. 68 (12) (2016) 3002–3009.
[31] S.P. Juraschek, C. Yokose, N. McCormick, E.R. Miller 3rd, L.J. Appel, H.K. Choi, Effects of dietary patterns on serum urate: results from a randomized trial of the effects of diet on hypertension, Arthritis Rheumatol. 73 (6) (2021) 1014–1020.
[32] S.P. Juraschek, E.R. Miller 3rd, B. Wu, K. White, J. Charleston, A.C. Gelber, S.K. Rai, K.A. Carson, L.J. Appel, H.K. Choi, A randomized pilot study of DASH patterned groceries on serum urate in individuals with gout, Nutrients 13 (2) (2021).
[33] Y. Gao, L.F. Cui, Y.Y. Sun, W.H. Yang, J.R. Wang, S.L. Wu, X. Gao, Adherence to the dietary approaches to stop hypertension diet and hyperuricemia: a cross-sectional study, Arthritis Care Res. 73 (4) (2021) 603–611.
[34] C. Chrysohoou, J. Skoumas, C. Pitsavos, C. Masoura, G. Siasos, N. Galiatsatos, T. Psaltopoulou, C. Mylonakis, A. Margazas, S. Kyvelou, et al., Long-term adherence to the Mediterranean diet reduces the prevalence of hyperuricaemia in elderly individuals, without known cardiovascular disease: the Ikaria study, Maturitas 70 (1) (2011) 58–64.
[35] M.D. Kontogianni, C. Chrysohoou, D.B. Panagiotakos, E. Tsetsekou, A. Zeimbekis, C. Pitsavos, C. Stefanadis, Adherence to the Mediterranean diet and serum uric acid: the ATTICA study, Scand. J. Rheumatol. 41 (6) (2012) 442–449.
[36] M. Chatzipavlou, G. Magiorkinis, L. Koutsogeorgopoulou, D. Kassimos, Mediterranean diet intervention for patients with hyperuricemia: a pilot study, Rheumatol. Int. 34 (6) (2014) 759–762.
[37] C. Yokose, N. McCormick, S.K. Rai, N. Lu, G. Curhan, D. Schwarzfuchs, I. Shai, H.K. Choi, Effects of low-fat, mediterranean, or low-carbohydrate weight loss diets on serum urate and cardiometabolic risk factors: a secondary analysis of the dietary intervention randomized controlled trial (direct), Diabetes Care 43 (11) (2020) 2812–2820.
[38] Y.J. Jeong, S. Park, D.K. Yon, S.W. Lee, K. Tizaoui, A. Koyanagi, L. Jacob, K. Kostev, E. Dragioti, J. Radua, et al., Global burden of gout in 1990-2019: a systematic analysis of the Global Burden of Disease study 2019, Eur. J. Clin. Invest. 53 (4) (2023), e13937.
[39] J. Wu, Y. Zhou, H. Hu, D. Yang, F. Yang, Effects of β-carotene on glucose metabolism dysfunction in humans and type 2 diabetic rats, Acta Mater. Med. (2022) 1.
[40] Y. Han, K. Han, Y. Zhang, X. Zeng, Serum 25-hydroxyvitamin D might be negatively associated with hyperuricemia in U.S. adults: an analysis of the National Health and Nutrition Examination Survey 2007-2014, J. Endocrinol. Invest. 45 (4) (2022) 719–729.
[41] O. Brzezińska, F. Styrzyński, J. Makowska, K. Walczak, Role of vitamin C in prophylaxis and treatment of gout-A literature review, Nutrients 13 (2) (2021).
[42] S.P. Juraschek, J.M. Gaziano, R.J. Glynn, N. Gomelskaya, V.Y. Bubes, J.E. Buring, R.H. Shmerling, H.D. Sesso, Effects of vitamin C supplementation on gout risk: results from the Physicians' Health Study II trial, Am. J. Clin. Nutr. 116 (3) (2022) 812–819.
[43] Y. Yang, W. Piao, K. Huang, H. Fang, L. Ju, L. Zhao, D. Yu, Y. Ma, Dietary pattern associated with the risk of hyperuricemia in Chinese elderly: result from China nutrition and health surveillance 2015-2017, Nutrients 14 (4) (2022).
[44] M.M. Kiyani, M.A. Butt, H. Rehman, H. Ali, S.A. Hussain, S. Obaid, M. Arif Hussain, T. Mahmood, S.A.I. Bokhari, Antioxidant and anti-gout effects of orally administered zinc oxide nanoparticles in gouty mice, J. Trace Elem. Med. Biol. 56 (2019) 169–177.
[45] X. Sun, J. Wen, B. Guan, J. Li, J. Luo, J. Li, M. Wei, H. Qiu, Folic acid and zinc improve hyperuricemia by altering the gut microbiota of rats with high-purine diet-induced hyperuricemia, Front. Microbiol. 13 (2022), 907952.
[46] H. Wu, Y. Wang, J. Huang, Y. Li, Z. Lin, B. Zhang, Rutin ameliorates gout via reducing XOD activity, inhibiting ROS production and NLRP3 inflammasome activation in quail, Biomed. Pharmacother. 158 (2023), 114175.
[47] Y.M. Roman, Moving the needle in gout management: the role of culture, diet, genetics, and personalized patient care practices, Nutrients 14 (17) (2022).
[48] Y. Feng, Y. Yu, Z. Chen, L. Wang, J. Ma, X. Bai, Y. Sun, D. Wang, Effects of β-carotin and green tea powder diets on alleviating the symptoms of gouty arthritis and improving gut microbiota in C57bl/6 mice, Front. Microbiol. 13 (2022), 837182.
[49] M. Dehlin, S. Muller, C. Mallen, A.J. Landgren, L. Watson, L. Jacobsson, E. Roddy, Sex and country differences in gout: cross-country comparison between Sweden and the UK, Scand. J. Rheumatol. (2023) 1–10.
[50] K. Lin, N. McCormick, C. Yokose, A.D. Joshi, N. Lu, G.C. Curhan, T.R. Merriman, K.G. Saag, P.M. Ridker, J.E. Buring, et al., Interactions between genetic risk and diet influencing risk of incident female gout: discovery and replication analysis of four prospective cohorts, Arthritis Rheumatol 75 (6) (2023) 1028–1038.
[51] A. Tin, J. Marten, V.L. Halperin Kuhns, Y. Li, M. Wuttke, H. Kirsten, K.B. Sieber, C. Qiu, M. Gorski, Z. Yu, et al., Target genes, variants, tissues and transcriptional pathways influencing human serum urate levels, Nat. Genet. 51 (10) (2019) 1459–1474.
[52] H. Yamanaka, Gout and hyperuricemia in young people, Curr. Opin. Rheumatol. 23 (2) (2011) 156–160.
[53] R.J. Johnson, B.A. Rideout, Uric acid and diet–insights into the epidemic of cardiovascular disease, N. Engl. J. Med. 350 (11) (2004) 1071–1073.
[54] M. Tomita, S. Mizuno, K. Yokota, Increased levels of serum uric acid among ex-smokers, J. Epidemiol. 18 (3) (2008) 132–134.
[55] B. Nieradko-Iwanicka, The role of alcohol consumption in pathogenesis of gout, Crit. Rev. Food Sci. Nutr. 62 (25) (2022) 7129–7137.
[56] A.A.S. Syed, A. Fahira, Q. Yang, J. Chen, Z. Li, H. Chen, Y. Shi, The relationship between alcohol consumption and gout: a mendelian randomization study, Genes 13 (4) (2022).
[57] C. Yokose, N. McCormick, H.K. Choi, The role of diet in hyperuricemia and gout, Curr. Opin. Rheumatol. 33 (2) (2021) 135–144.
[58] A. Danve, S.T. Sehra, T. Neogi, Role of diet in hyperuricemia and gout, Best Pract. Res. Clin. Rheumatol. 35 (4) (2021), 101723.