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Dietary inflammatory potential is linked to cardiovascular disease risk burden in the US adult population

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Abstract

Background—Dietary guidelines are a key tool in the public health quiver. Single nutrients have been linked to cardiovascular diseases, but existing metrics do not capture the overall effect of diet on inflammatory diseases. The aim of this study was to examine the association between dietary inflammatory potential and cardiovascular diseases risk factors (CVD-RFs) in a nationally-representative sample of non-institutionalized US adults using data from the continuous National Health and Nutrition Examination Survey (NHANES) (2007–2012).

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*These authors take responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation

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Methods and Results—A sample of 7,880 non-institutionalized US adults aged ≥20 years provided data on dietary habits and CVD-RFs (obesity; diabetes mellitus; hypertension; hypercholesterolemia). The total number of CVD-RFs was summed for each individual to create a CVD-RF morbidity index (range 0–4) as the outcome variable, used both as ordinal and dichotomous (no CVD-RFs versus at least one CVD-RF) variables. The association between the Dietary Inflammatory Index (DII) and at least one CVD-RF was dose-dependent, with participants in the 3rd and 4th quartile of DII (i.e., more pro-inflammatory dietary habits) being 1.37 (95%CI=1.11–1.68) and 1.50 (95%CI=1.19–1.90) times more likely, respectively, to have at least one CVD-RF, as compared to participants in the 1st quartile of DII scores. Similar results were obtained for the ordinal logistic regression using the CVD-RF morbidity index as the outcome.

Conclusions—Among US adults aged ≥20 years, pro-inflammatory dietary patterns, as assessed by the DII, were associated with increased odds for CVD-RFs. Dietary guidelines aimed at lowering the DII may reduce the CVD-RF burden in US adults.

Keywords

NHANES; cardiovascular diseases; diet; inflammation; risk factors

Introduction

According to the World Health Organization (WHO) and other sources, individuals with cardiovascular diseases (CVDs) have the highest mortality risk globally [1, 2]. Recent data from the Global Burden of Disease (GBD) study 2013 indicate that CVDs are the most prevalent non-communicable diseases and the major cause for disability worldwide [3]. Nonetheless, CVD risk factors (CVD-RFs) such as obesity and hypertension are on the rise, supporting a trend for increased CVD-related morbidity and mortality [4]. This rise in CVD morbidity and mortality has sparked a multitude of investigations to identify simple, yet efficacious interventions to prevent CVD at every life stage [5].

The beneficial role of healthy dietary habits in reducing CVD burden is well known [6]. Epidemiologic studies have shown that unhealthy dietary habits, such as high fat consumption, are related to increased CVD burden [7, 8], while holistic healthy dietary patterns (e.g., high intake of fruits, vegetables, legumes, whole grains, fish, and low-fat dairy products), as well as specific antioxidant food items (e.g., n-3 fatty acids, flavonoids, etc.) have been associated with lower overall CVD burden [9–11]. The main pathway that is believed to explain the beneficial effect of healthy nutrition on CVD burden is through the regulation of chronic inflammation [12, 13]. Protective dietary patterns have been reported to reduce low-grade inflammation and oxidative stress, as well as improvement in endothelial function [14, 15].

Despite some progress on the effect of diet on these CVD-related pathogenic mechanisms, the quantification of effects has been challenging. Existing studies have evaluated the effect of dietary habits on human health following either the classical approach of assessing single food items (e.g., fish consumption) and nutrients (e.g., flavonoids), or by using a holistic dietary approach, such as the Mediterranean diet [16] or the Dietary Approaches to Stop Hypertension (DASH) diet [17]. While the holistic dietary approach is strongly

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recommended for disease prevention [16],[18], these dietary pattern indices are not designed to capture dietary inflammatory potential. Cavicchia and colleagues [19] first proposed the Dietary Inflammatory Index (DII) in 2009 on work conducted beginning in 2004 as a means to assess dietary inflammatory potential. Shivappa and colleagues [20] proposed the new, refined literature-based, DII in 2013. Using the new formulation, high DII scores have been shown to be associated with various CVD risk factors such as glucose intolerance and dyslipidemia components of the metabolic syndrome in two cross-sectional studies and one cohort study; with anthropometric measurements and established cardiovascular disease [21–25]. Furthermore, a more pro-inflammatory diet based on the DII has been associated with increased risk for all-cause mortality as well as CVD mortality[26]. Given the importance of dietary habits as a set of modifiable CVD risk factors that can improve population health in a direct and cost-effective manner, the aim of the present study was to assess the association between the DII scores and the CVD risk burden in a nationally-representative sample of non-institutionalized US adults using data from the National Health and Nutrition Examination Survey (NHANES) (2007–2012).

Methods

The survey

Data from the 2007–2008, 2009–2010, and 2011–2012 continuous NHANES were analyzed. The NHANES is a nationally-representative cross-sectional survey conducted by the National Center for Health Statistics (NCHS) and Centers for Disease Control and Prevention. For the continuous NHANES, a complex multistage probability sampling design has been used since 1999 to select participants representative of the non-institutionalized US population[27].

Ethics, consent and permissions

The NCHS Research Ethics Review Board (ERB) approved the study protocol of 2007–2008, 2009–2010 (protocol 2005–06), and 2011–2012 (protocol 2011–17) NHANES and all participants provided written informed consent.

Dietary assessment and Dietary Inflammatory Index (DII)

Trained interviewers conducted 24-hour dietary recall assessments using the US Department of Agriculture's (USDA's) Automated Multiple-Pass Method [28]. Dietary data included detailed descriptions of all foods consumed and the quantities eaten. A detailed description of the dietary interview methodology is provided in the NHANES Dietary Interviewer's Training Manual [29].

The calculation of the DII in this study sample was based on the methodology proposed and validated by Shivappa and colleagues [20]. The DII was constructed based on a systematic review of studies investigating the effect of various food components (i.e., 45 food parameters) on specific pro-inflammatory and inflammatory biomarkers [i.e., interleukin (IL)-10, IL-4, IL-6, IL-1β, tumor necrosis factor (TNF)-α and C-reactive protein (CRP)]. A specific z-score for each food item was computed, as previously described, and each food component's z-score was converted to the centered percentile score for each individual and

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then was multiplied by the specific food item effect score. With this procedure, each individual's specific food component (DII score) was calculated. Finally, all of the specific food components' DII scores were then summed to generate the total DII score for each participant. Higher DII scores correspond to more pro-inflammatory diets [20].

Based on the 1st NHANES dietary recall interview, a total of 27 food components were used for the calculation of the DII. These were: carbohydrates, proteins, fats, alcohol, fibers, cholesterol, saturated fatty acids, monounsaturated fatty acids, polyunsaturated fatty acids, omega 3, omega 6, niacin, thiamin, riboflavin, vitamin B6, vitamin B12, iron, magnesium, zinc, selenium, vitamin A, vitamin C, vitamin D, vitamin E, folic acid, beta carotene. Quartiles of the DII score also were calculated.

CVD risk factors (CVD-RFs)

Four CVD-RFs were assessed:

1. *Obesity* was defined as BMI≥30/kg^2 [30]. Weight and height measured at the mobile examination centers (MECs) were used for calculating BMI.
2. *Diabetes mellitus* (type 2) was defined as either: (a) glycated hemoglobin A1C≥6.5; fasting blood glucose levels ≥120 mg/dl; or (b) self-reported prior diagnosis of diabetes, based on the American Diabetes Association diagnostic criteria.
3. *Hypertension* referred to either: (a) Systolic blood pressure ≥140 mmHg; diastolic blood pressure ≥90 mmHg; or (b) Self-reported prior diagnosis of hypertension.
4. *Hypercholesterolemia* was defined by the presence of at least one of: total serum cholesterol levels ≥200 mg/dL; or self-reported prior diagnosis of hypercholesterolemia [6].

The total number of these CVD-RFs was summed for each individual to create a CVD-RF morbidity index (range 0–4). This variable was used as an ordinal variable and as a dichotomous variable (no CVD-RFs vs. at least one CVD-RF) in the analysis.

Medical conditions and other covariates

The presence of heart disease (i.e., at least one of: congestive heart failure; coronary heart disease; angina; or myocardial infarction) was ascertained by self-reported prior diagnosis of these conditions. Depression was assessed by the 9-item Patient Health Questionnaire (PHQ-9) depression scale which was based on the frequency of symptoms in the past 2 weeks. The scale ranged from 0–27 with scores of 0–4, 5–9, 10–14, 15–19, ≥20 corresponding to no depression, mild, moderate, moderately severe, and severe depression respectively [31]. In line with a previous publication, depression was defined as a score ≥10 [31].

The other covariates used for adjustment were sex, age, race/ethnicity (non-Hispanic White, Hispanic, non-Hispanic Black, other), wealth (i.e., in relation to the poverty line), highest education achieved (<9th grade, 9–11th grade, high school, some college, ≥college graduate),

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current marital status (married/cohabiting, widowed/divorced/separated, never married), physical activity (low, moderate, high) and current smoking (not at all, some days, everyday). Wealth was assessed using the ratio of family income to poverty [i.e., Poverty Income Ratio (PIR)] which was calculated based on the poverty guidelines of the Department of Health and Human Services. A PIR<1.0 corresponds to a family income level below the official poverty threshold [32]. Level of physical activity was assessed with the Global Physical Activity Questionnaire using conventional cut-offs (http://www.who.int/chp/steps/GPAQ/en/).

Statistical analysis

Analyses were performed with Stata® version 13.1 (Stata Corp LP, College Station, Texas). The analysis was restricted to participants ≥20 years old, as the focus of this paper was on adults. Furthermore, approximately half of the sample was randomly assigned to a morning examination session during which a fasting blood sample was drawn. We restricted the sample to those who had values for fasting blood glucose to allow for the systematic and unbiased assessment of all CVD-RFs for all individuals included in the current study.

Participants are classified according to percentages or means (SDs) by the presence of at least one CVD-RF (CVD status). Comparisons of continuous and categorical variables by CVD-RF status were performed using Student's *t*-tests and chi^2 tests respectively. We conducted multivariable binary and ordinal logistic regression analyses with CVD-RF as the outcome. The outcome was at least one CVD-RF for the former, and the CVD-RF morbidity index (total number of CVD-RFs ranging from 0–4) for the latter. The exposure variable was the DII, which was used both as continuous and categorical (quartiles) variables. All analyses were adjusted for age, sex, race, wealth in relation to poverty threshold, education, marital status, smoking, physical activity, heart disease, and depression. All analyses accounted for the complex study design, and appropriate sampling weights were used to account for unequal probability of selection stemming from study design and non-response to generate nationally-representative estimates. Standard errors were calculated based on Taylor series linearization [33]. The level of statistical significance was set at P<0.05.

Results

The total analytical sample included 7,880 individuals ≥20 years of age who had information on fasting blood glucose. The prevalence of at least one CVD-RF was 76.0% (95%CI=74.5%–77.5%) with the prevalence (95%CI) of one, two, three, and four CVD-RFs being 32.4% (30.8%–34.0%), 25.7% (24.2%–27.2%), 13.0% (12.0%–14.0%), and 4.9% (4.3%–5.7%), respectively.

The sample characteristics by the presence or absence of at least one CVD-RF are summarized in Table 1. Advanced age, ethnicity, poverty, lower levels of education, marital status, smoking status, lower physical activity, heart disease, and depression were all associated with a significantly higher likelihood of having at least one CVD-RF. [Table 1]

The association between the inflammatory potential of dietary habits and at least one CVD-RF as estimated by multivariable binary logistic regression is shown in Table 2. Compared to

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those with very anti-inflammatory diets (1st quartile of DII), participants with more pro-inflammatory dietary habits (3rd and 4th quartile) were 1.37 (95%CI=1.11–1.68) and 1.50 (95%CI=1.19–1.90) times more likely to have at least one CVD-RF, respectively. When the DII was included in the model as a continuous variable, a one-unit increase in the DII (shift to more pro-inflammatory dietary habits) was associated with 1.08 (95%CI=1.03–1.13; p=0.001) greater odds of having at least one CVD-RF (*data shown only in text*). [Table 2]

The results were similar when the outcome was the number of CVD-RFs, with more pro-inflammatory dietary habits being significantly associated with higher odds for being in a higher category of CVD-RFs (OR 1.17–1.39) (Table 3). Compared to those following the most anti-inflammatory diet (1st quartile of DII), participants with more pro-inflammatory dietary habits (2nd, 3rd and 4th quartile) were 1.16 (95%CI=1.01–1.35; p=0.04) and 1.39 (95%CI=1.19–1.62; p<0.001) times more likely to be in a higher category of CVD-RFs. The OR of the DII when included in the model as a continuous variable was 1.07 (95%CI=1.03–1.10; p<0.001) (data *shown only in text*). [Table 3]

Discussion

The present work revealed a positive association between higher DII scores (more pro-inflammatory dietary habits) and CVD-RF burden in US adults aged ≥20 years that persisted after extensive adjustment for potential confounders. Translating the present findings into numbers, participants on the upper quartile of pro-inflammatory diet were 50% more likely to have a CVD risk factor as compared to participants in the lower percentile. Adjusted analysis considering the quartiles of DII scores as the exposure showed that more pro-inflammatory dietary habits are associated with CVD-RF burden in a dose-dependent fashion. This finding supports the role of diet-associated inflammation in determining CVD risk that has been reported previously for specific nutrients [34, 35] or dietary schedules[16, 17].

It has been reported that a meat-centered; i.e., “Western” diet that departs from the traditional healthy dietary patterns is strongly related to chronic inflammation [36–38]. On the contrary, a healthy diet rich in vegetable is inversely associated with various inflammatory markers [39, 40]. Inflammation and oxidative stress are determined by individuals’ nutrition and subsume pathways that are strongly related to CVD risk [34]. Previous studies have reported the role of healthy dietary habits in determining distinct CVD risk factors (e.g., diabetes, obesity, hypercholesterolemia). For example food patterns either rich in fiber, or in whole-grain cereals are associated with lower odds of diabetes, obesity and hypercholesterolemia while high-fat dietary patterns seem to be related with higher likelihood of hypercholesterolemia [41–43]. Moreover, it has been proposed that various antioxidant nutrition components (such as, flavonoids, polyphenols, vitamins) as well as specific fatty acids (unsaturated or poly-unsaturated fatty acids, n-3 fatty acids, etc.), are involved in nutrition pathways that could reduce low-grade systemic inflammation [34, 44]. Previous NHANES [45] and other studies [46–49] have validated the DII against various inflammatory markers (i.e., CRP) and have shown a high level of correlation between the two.

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Despite the fact that previous studies have established the association between individual CVD-RFs and dietary habits [44, 50–52], the exact interrelation between abnormal CVD-RF profiles, healthy eating and low-grade inflammation still remains unclear. Results from the present analysis indicate that a pro-inflammatory diet is associated with increased odds of CVD-RF burden. Furthermore, the computation of DII scores allows for the direct quantification of diet's inflammatory potential and can be utilized as a cost-effective tool for designing population-level dietary guidelines. Specifically, common dietary recommendations can be enhanced by incorporating the DII formulation. This can be summarized as follows: Increased saturated and trans fatty acids intake as well as low intake of dietary fiber, fruits, vegetables, vitamins and flavonoids will result in a more pro-inflammatory diet and adherence to an unhealthy dietary pattern. On the contrary, high consumption of fruits, vegetables, whole grains as well as high intake of herbs and spices in parallel with limited intake of saturated and poly-unsaturated fatty acids will indicate a highly anti-inflammatory nutrition related with the adherence to a healthier diet [53, 54]. The clear delineation of the 8 pro-inflammatory and 37 anti-inflammatory parameters makes recommendations to alter a ubiquitous risk factor in human health relatively easy to operationalize. Doing so should be taken into account by public health policy-makers who seek to develop direct and cost-effective actions for reducing the burden of cardiometabolic diseases, and reducing associated health care costs.

Considering the high prevalence of cardiovascular diseases, the increased risk for mortality, and their overall burden in health care-costs, minimizing pro-inflammatory dietary habits, may be an important component in public health planning to reduce suffering and associated costs. Based on the findings of the present study, prospective and interventional studies are necessary to assess the effect of public health strategies that address diet's inflammatory potential as a key part of the dietary guidelines to reduce CVD-RF burden.

Strengths and limitations

The present study has notable strengths. Previous studies in various populations (Europe and North America) have reported associations between the DII and cardiovascular health [21, 23, 24, 44]. However these efforts have assessed the DII's role in isolated CVD risk factors or in established CVDs. The present study interrogated the role of DII on CVD-RF metabolic burden in a nationally-representative US sample and elucidated the increased and independent effect of pro-inflammatory dietary habits in individuals´ accumulated CVD-RFs metabolic profiles. In addition, the dietary measures utilized in the present study were specifically designed to capture the overall diet's inflammatory potential not only from a research perspective but also in a way that is readily usable for implementation in public health interventions. In terms of limitations, one is, the study's cross-sectional design and the inability to establish causal relationships based on temporality (one of the nine Criteria of Judging Causality) [55, 56]. Moreover, our findings share the limitations of epidemiological studies that rely on self-reported measures of dietary intake. Also, the cumulative CVD-RF "morbidity index", developed here by simply adding the presence of four classic CVD risk factors pertaining to individuals may not accurately estimate the CVD burden of the US population. The absence of other, classical and novel modifiable CVD risk factors, such as smoking and sedentary lifestyle, socioeconomic and education level in the

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CVD-RF score may also be considered a limitation; however, nutrition has limited influence on these cardiometabolic factors and these factors were adjusted for in the analytical models.

Conclusions

Among US adults aged 20 years or older, pro-inflammatory dietary patterns, as assessed by the DII, were associated with increased odds for CVD-RFs. Dietary guidelines aimed at lowering the DII may reduce the CVD-RF burden in US adults.

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Table 1

Sample characteristics by the presence or absence of at least one cardiovascular disease risk factor (CVD-RF)[a]

Characteristic	Category	No CVD-RF	CVD-RF	P-value[b]
Age (years)	Mean (SE)	34.8±0.42	50.9±0.33	<0.001
Sex	Male	47.5	48.4	0.58
Race/ethnicity	Non-Hispanic white	65.5	68.9	<0.001
	Hispanic	15.3	13.3	
	Non-Hispanic black	9.9	11.6	
	Other	9.2	6.1	
Wealth	Poor	17.0	14.3	0.002
Education	<9th grade	4.5	6.9	<0.001
	9–11th grade	9.7	13.0	
	High school	20.5	22.8	
	Some college	31.1	29.5	
	≥College graduate	34.1	27.8	
Marital status	Married/cohabiting	58.3	65.6	<0.001
	Widowed/divorced/separated	9.7	20.5	
	Never married	32.0	13.9	
Smoking status	Never	60.6	54.1	<0.001
	Quit	16.1	26.9	
	Current	23.3	18.9	
Physical activity	High	44.1	31.0	<0.001
	Moderate	21.9	21.5	
	Low	34.1	47.5	
Heart disease	Yes	0.6	9.2	<0.001
Depression	Yes	5.2	8.1	0.001

Data are percent of individuals with that sample characteristic among those with or without CVD-RFs unless otherwise stated.

[a] CVD-RFs included obesity, diabetes, hypertension, and hypercholesterolemia.

[b] P-values were obtained by Chi-square tests for all variables with the exception of age (Student's *t*-test).

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Table 2

The association of inflammatory potential of dietary habits and other factors with at least one cardiovascular disease risk factor[a] estimated by multivariable binary logistic regression

Characteristic	Category	OR	95%CI
Dietary Inflammatory Index (DII)	1st (anti-inflammatory)	1.00	
(quartiles)	2nd	1.14	[0.91,1.43]
	3rd	1.37**	[1.11,1.68]
	4th (pro-inflammatory)	1.50***	[1.19,1.90]
Age (years)[b]	per year	1.08***	[1.07,1.09]
Sex	Male	1.00	
	Female	0.85	[0.71,1.02]
Race/ethnicity	Non-Hispanic white	1.00	
	Hispanic	1.32**	[1.05,1.65]
	Non-Hispanic black	1.42***	[1.17,1.72]
	Other	0.95	[0.69,1.32]
Wealth	Not poor	1.00	
	Poor	1.16	[0.90,1.50]
Education	<9th grade	1.00	
	9–11th grade	1.53	[1.12,2.08]
	High school	1.17	[0.86,1.59]
	Some college	1.39*	[0.99,1.95]
	≥College graduate	1.01	[0.69,1.46]
Marital status	Married/cohabiting	1.00	
	Widowed/divorced/separated	0.99	[0.75,1.29]
	Never married	0.88	[0.73,1.06]
Smoking status	Never	1.00	
	Quit	1.05	[0.84,1.30]
	Current	0.89	[0.71,1.10]
Physical activity	High	1.00	
	Moderate	1.17	[0.95,1.44]
	Low	1.22*	[1.01,1.48]
Heart disease	Yes vs. No	4.21***	[2.26,7.84]
Depression	Yes vs. No	1.44*	[1.03,2.02]

Abbreviation: OR Odds ratio; CI Confidence interval
Model is mutually adjusted for all variables in the table.

[a] Cardiovascular disease risk factors included obesity, diabetes, hypertension, and hypercholesterolemia.

[b] Age was included in the model as a continuous variable.

* p<0.05,

** p<0.01,

*** p<0.001

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Table 3

The association between inflammatory potential of dietary habits and the number of cardiovascular disease risk factors[a] estimated by multivariable ordinal logistic regression

Dietary Inflammatory Index (DII; quartiles)	OR	95%CI
1st (anti-inflammatory)	1.00	
2nd	1.17*	[1.01, 1.35]
3rd	1.39**	[1.19, 1.63]
4th (pro-inflammatory)	1.39**	[1.15, 1.67]

Abbreviation: OR Odds ratio; CI Confidence interval

Models are adjusted for age, sex, race, poverty, education, marital status, smoking, physical activity, heart disease, and depression.

[a]Cardiovascular disease risk factors included obesity, diabetes, hypertension, and hypercholesterolemia. The total number of these risk factors was calculated (range 0–4) for each individual and used as the outcome.

*p<0.05,

**p<0.001