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Association between dietary inflammatory index and serum C-reactive protein concentrations in the Japan Collaborative Cohort Study

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ABSTRACT

Diet plays an important role in the regulation of chronic inflammation, which is linked to cardiovascular disease (CVD) and several cancers. The dietary inflammatory index (DII®) was developed to estimate the inflammatory potential of an individual's diet. We examined the association between DII scores and serum high-sensitivity C-reactive protein (hs-CRP) concentrations using the baseline data from the Japan Collaborative Cohort Study (JACC Study). Data were from 1176 control subjects (650 men and 526 women) in a nested case-control study of several cancers and CVD in the JACC Study who were free of cancer and CVD at baseline. DII scores were calculated from 26 food parameters that were derived from a validated food frequency questionnaire administered at the baseline. Energy-adjusted DII scores were calculated using the residual method. Serum hs-CRP concentrations were measured by latex-enhanced nephelometry or enzyme-immunoassay. In multivariable logistic regression analysis adjusting for potential confounders including sex, age, smoking habits, drinking habits, body mass index, and history of hypertension, the odds ratio (OR) and 95% confidence intervals (CI) for high serum hs-CRP concentrations (>1.0 mg/L) was significantly higher in the highest versus the lowest DII quartile ($OR_{Quartile4vs1}$ = 1.32, 95% CI = 1.01 to 2.52). Likewise, a 1-point increase in DII score was associated with a 14% increased risk of high serum hs-CRP concentrations ($OR_{Continuous}$ = 1.09, 95%CI = 1.01 to 1.19). A pro-inflammatory diet, as represented by high DII scores, was associated with high serum hs-CRP concentrations in this Japanese population.

Keywords: dietary inflammatory index, serum hs-CRP concentrations, Japanese population, inflammation, cross-sectional study

Abbreviations:
BMI: body mass index

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CHD: coronary heart disease
CI: confidence interval
CVD: cardiovascular disease
DII: dietary inflammatory index
FFQ: food frequency questionnaire
hs-CRP: high-sensitivity C-reactive protein
IL: interleukin
JACC Study: Japan Collaborative Cohort Study
OR: odds ratios

INTRODUCTION

Diet is well known to play a major role in regulating chronic inflammation[1,2] that is involved in the etiology and progression of most chronic diseases.[3] The Western dietary pattern, characterized by high intakes of red and processed meat, refined grains, and high-fat dairy products, has consistently been associated with increased markers of inflammation.[4,5] On the other hand, a diet rich in vegetables and fruits, including the Mediterranean diet, have been shown to reduce inflammation.[6,7] Specific nutrients such as fiber,[8] vitamin C,[9] beta-carotene,[9] and n-3 PUFAs[10] also have been shown to be associated with lower concentrations of inflammation.

Shivappa et al[11] developed the dietary inflammatory index (DII®), a literature-derived, population-based dietary score summarizing the effect of dietary parameters on six inflammatory biomarkers (IL-1β, IL-6, TNF-α or C-reactive protein (CRP), IL-4 and IL-10). According to a comprehensive review of the literature published from 1950 to 2010 a total of 45 dietary parameters, including micro and macro nutrients, flavonoids, and individual food items, were associated with the six inflammatory biomarkers. The DII can be used to estimate the inflammatory potential of diet as estimated by a variety of assessment methods, and has been shown to be associated with serum inflammation markers such as CRP and IL-6 in Western and Middle Eastern countries.[12-17] Hence, the DII appears to be a useful tool for assessing the inflammatory potential of the diet that can be applied to any population-based study anywhere in the world.

Japanese have lower concentrations of CRP than their Western counterparts, in part because they have lower concentrations of adiposity and their BMI is lower.[18] Japanese also have lower mortality from coronary heart disease (CHD).[19] To date, there are few studies that have examined the association between DII scores and serum CRP concentrations in a Japanese population. Given what has been observed in other countries, it would be interesting to explore the association between DII scores and inflammation markers in Japanese adults. To examine the association between DII scores and serum high-sensitivity C-reactive protein (hs-CRP) concentrations in Japanese, we conducted a cross-sectional study using the data from the Japan Collaborative Cohort Study (JACC Study).

MATERIALS AND METHODS

Study subjects

The baseline survey of the JACC Study, which was conducted from 1988 to 1990, involved subjects aged 40 to 79 years, living in 45 communities across Japan. Methodologic details have been described elsewhere.[20,21] A total of 39,242 participants were administered a questionnaire on life-style and donated serum samples at baseline. Of these, 818 cases and 1552 controls

were chosen to examine the associations between serum hs-CRP concentrations and the risk for lung, stomach, colorectal[22] and gallbladder cancers, and cardiovascular disease (CVD).[23] Of the 1552 control subjects, we excluded the following subjects; 179 with a self-reported history of cancer, CHD, cerebrovascular disease, kidney disease, and diabetes mellitus at baseline that may affect the outcome; 180 subjects missing any of the measurements including DII scores; and 17 subjects with serum hs-CRP > 10mg/L. A total of 1176 control subjects (650 men and 526 women) were eligible for the present analysis. There was no subject with implausibly high or low total energy intakes (<500 or >3,500 kcal/d) among study subjects. Informed consent was obtained individually from most subjects, except in a few study areas where informed consent was provided at the group level, and data confidentiality was explained to community leaders. The study protocol was approved by the Ethics Committees of Hokkaido University (approval number; 14-044), which is where the central secretariat of the JACC study is located.

Data collection

Information on lifestyle at baseline was collected using a self-administered questionnaire, that covered age, sex, height, weight, medical history of cancer (yes or no), CHD (yes or no), cerebrovascular disease (yes or no), hypertension (yes or no), kidney disease (yes or no), and diabetes mellitus (yes or no), smoking habits (never, ex-smoker, and current smoker), drinking habits (nondrinker, Ex-drinker, and current drinker). A food frequency questionnaire (FFQ)[24] was used to ascertain the average intake frequency of 40 food items in the past year. For 33 foods or dishes, we asked about the average intake frequency without specifying portion size. We used the following 5 response choices: almost never; 1–2 times a month; 1–2 times a week; 3–4 times a week; and almost every day. For rice and miso soup, we asked about the number of bowls or cups consumed each day. Non-alcoholic beverages (green tea, black tea, oolong tea, and coffee) were assessed using five frequency categories: almost never; 1–2 cups/month; 1–2 cups/week; 3–4 cups/week; and almost every day. For alcoholic beverages, we inquired about the frequency of consumption (<1 time/week, 1–2 times/week, 3–4 times/week, and almost daily) and the usual amount consumed on each occasion. The FFQ was validated by comparing to four 3-day weighted dietary records over a 1-year period as a standard.[25] The daily intake of nutrients was calculated by multiplying the intake frequency of each item by its nutrient content per serving and totaling the nutrient intake for all food items queried on the FFQ.[25]

The DII was developed to assess the inflammatory potential of an individual's overall diet.[11] The nutrients data derived from the FFQ was used to calculate the DII scores for all study subjects. The details the design and development of the DII scoring algorithm have been described elsewhere.[26] The food parameters were scored as follows: "+1" was assigned if the effects were pro-inflammatory (significantly increased IL-1β, IL-6, TNF-α, or CRP, or decreased IL-4 or IL-10); '–1' was assigned if the effects were anti-inflammatory (significantly decreased IL-1β, IL-6, TNF-α or CRP, or increased IL-4 or IL-10); and '0' was assigned if no significant association was observed between the food parameter and the above inflammatory markers.[11] These scores were weighted based on study design. To avoid the arbitrariness resulting from simply using raw consumption amounts, intakes of foods and nutrition were standardized to a representative range of dietary intake based on actual human consumption in 11 populations living in different countries across the world that provided an estimate of a mean and standard deviation for each parameter. These values were converted to a proportion (with values from 0 to 1). Each proportion was doubled, and then 1 was subtracted to achieve a symmetrical distribution around a mean of ≈0. Each of these values was then multiplied by an overall food parameter-specific inflammation score. All the food parameter-specific DII scores were summed to create the overall DII scores for each subject. Higher DII scores indicate more pro-inflammatory diets, while lower

DII scores represent anti-inflammatory diets. In this study, data were available for a total of 26 food parameters (carbohydrate, protein, total fat, alcohol, fiber, cholesterol, saturated fatty acid, monounsaturated fatty acid, polyunsaturated fatty acid, omega-3 fatty acid, omega-6 fatty acid, vitamin A, vitamin B1, vitamin B2, vitamin B6, vitamin B12, vitamin C, vitamin D, vitamin E, niacin, folic acid, beta-carotene, iron, magnesium, zinc, and tea) to calculate the DII scores.

Serum samples were stored at -80 degrees centigrade until biochemical analysis. Serum hs-CRP concentrations were measured by latex-enhanced nephelometry (BN Prospec nephrometer; Dade Behring, Tokyo, Japan) in the nested case-control study of CVD or enzyme-immunoassay (High sensitivity C-reactive protein enzyme immunoassay test kit, Diagnostic Automation Inc., USA) in nested case-control study of lung, stomach, colorectal, and gallbladder cancers. The inter-assay and intra-assay coefficients of variations (CVs) for hs-CRP of each kit were less than 10%, respectively.[23,27] The correlation between the enzyme-immunoassay and nephelometry assay according to the attached manual of ELISA assay kit was 0.96. These were satisfactory according to the CDC/AHA scientific criterion.[28] Based on previous work in a Japanese population, we defined more than 1.0 mg/L as high serum hs-CRP concentrations, which is recommended as a relevant cut-off point for high risk of future development of CVD in Japanese.[18]

Statistical analysis

Energy adjustment was performed using the residual method. Analysis of variance (ANOVA) was used to compare the mean values of continuous variable across quartiles of the DII scores and t-tests were used to compare the mean values of continuous variables between men and women. Because hs-CRP values had a lognormal distribution, the log-transformed value of hs-CRP was used for both simple t-tests and ANOVA. The chi-square test was used to compare percentages of categorical variables such as smoking habits, drinking habits, and hypertension across quartiles of the DII scores. We used multiple linear regression analysis to examine the association between DII scores and serum hs-CRP concentrations. Multivariable logistic regression analysis was used to estimate odds ratios (ORs) and 95% confidence intervals (CIs) for high serum hs-CRP concentrations (>1.0 mg/L). The distribution of DII scores was divided into quartiles and the ORs for high serum hs-CRP concentrations were compared by DII quartile [$DII_{(quartiles)}$], using the lowest quartile as a reference. ORs and 95%CIs were also estimated using continuous DII scores [$DII_{(continuous)}$]. We used sex, age, smoking habits, drinking habits, body mass index (BMI), total energy intake and history of hypertension as covariates as they may influence both dietary intake and inflammation and may either modify effects or cause spurious associations by confounding the effect of diet. A p value of <0.05 was considered statistically significant. The statistical software JMP ver. 12.2 (SAS Institute Inc., Cary, NC, USA) was used for statistical analysis.

RESULTS

The mean DII score was +0.83 (standard error: 0.04) and scores ranged from –3.61 (maximally anti-inflammatory) to +5.07 (maximally pro-inflammatory) among study subjects. Figure shows the distributions of DII score and serum hs-CRP concentration by sex. The DII scores were significantly higher in women than in men (mean ± standard deviation: 0.74±1.69 in men and 0.94±1.67 in women, $p = 0.04$). Men had significantly higher serum hs-CRP concentrations, smoking rates, and drinking rates compared to women (median and 25–75th percentiles: 0.50 (0.22–1.31) in men and 0.40 (0.16–0.85) in women, $p<0.001$). The percentages of serum hs-CRP concentrations of > 1.0 mg/L were 32.2% (n = 209) in men and 20.5% (n = 108) in women.

Table 1 shows the characteristics of the study subjects across quartiles of the DII scores. The percentage of subjects with high serum hs-CRP concentrations (>1.0 mg/L) was significantly higher in the highest quartile of the DII scores, though no significant differences in serum hs-CRP concentrations were observed across quartiles of DII scores. Dietary intakes of nutrients, except for carbohydrate and alcohol, significantly decreased with increase in DII scores. Dietary intakes of carbohydrate and alcohol were higher in the subjects with high DII scores. There also were no significant differences in age, BMI and percentages of men across quartiles of DII scores. In the multivariable linear regression analyses (Table 2), DII scores were positively associated with log serum hs-CRP concentrations ($\beta = 0.048$, 95%CI = 0.008 to 0.087), indicating that pro-inflammatory diet was associated with high serum hs-CRP. [Table 2] Similar results were obtained in men ($\beta = 0.085$, 95%CI = 0.002 to 0.106); however, despite a positive regression coefficient, no significant association was observed in women ($\beta = 0.041$, 95%CI = –0.002 to 0.103). Table 3 shows ORs and 95% CI for high serum hs-CRP concentrations (>1.0 mg/L) according to the DII scores. [Table 3] A significantly higher OR was observed in the highest quartile of DII scores ($OR_{Quartile4vs1} = 1.32$, 95%CI = 1.01 to 2.52) than in the lowest quartile in all subjects. A 1-point increase in DII scores [DII score (continuous)] was associated with a 9% increased risk of high hs-CRP concentrations (OR = 1.09, 95%CI = 1.01 to 1.19). In sex-stratified analyses, men had a significantly increased risk OR and 95%CI was observed in the highest quartile of DII scores compared to the lowest quartile ($OR_{Quartile4vs1} = 1.76$, 95%CI = 1.07 to 2.92). We obtained results of similar magnitude in women; however, they were not statistically significant. DII scores calculated by regressing separately by sex produced results similar to those obtained in multiple linear regression analysis and logistic regression analysis with data from men and women combined.

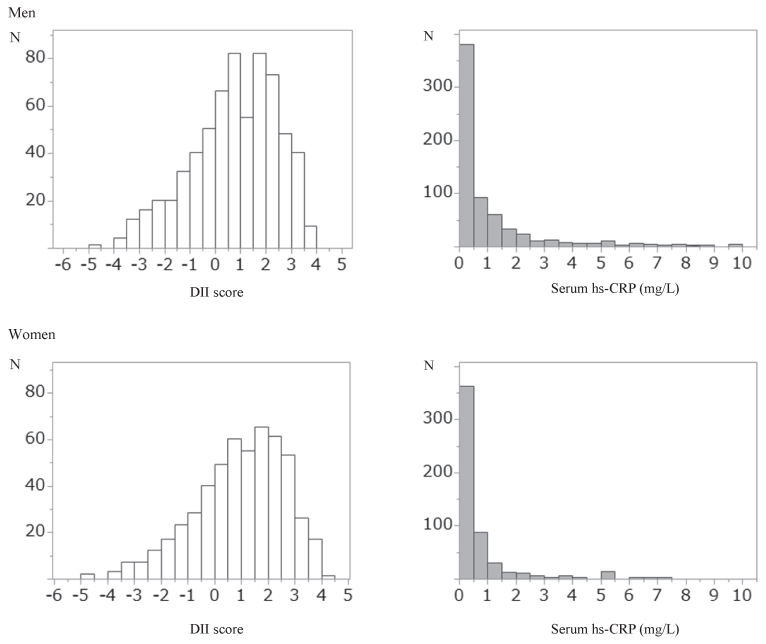

Fig. 1 Distributions of DII score and serum hs-CRP concentrations by sex
N: number, DII: dietary inflammatory index, hs-CRP: high sensitivity- C-reactive protein.

Table 1 Characteristics of the study subjects across quartiles of DII score

	DII score				
	Q1	Q2	Q3	Q4	p
n	294	294	294	294	
DII score range	<0.01	0.02 to 0.90	0.91 to 1.70	≧1.71	
DII score	–0.87 (0.67)	0.48 (0.26)	1.29 (0.23)	2.44 (0.60)	<0.001 [1]
Median	–0.81	0.48	1.28	2.28	
Men (%)	122 (41.5)	155 (52.7)	153 (52.0)	220 (74.8)	<0.001 [2]
Age (y)	64.3 (8.2)	64.0 (9.3)	63.6 (8.5)	61.8 (9.7)	0.01 [1]
BMI (kg/m^2)	22.9 (3.0)	22.5 (2.8)	22.5 (2.8)	22.6 (2.8)	0.20 [1]
hs-CRP (mg/L)	0.40 (0.17, 1.00)	0.47 (0.18, 0.96)	0.48 (0.22, 1.12)	0.49 (0.20, 1.25)	0.19 [3]
>1.0 mg/L n (%)	72 (24.5)	71 (24.2)	80 (27.2)	94 (29.7)	0.04 [4]
Current smoker n (%)	60 (20.4)	61 (20.8)	79 (26.9)	116 (39.5)	<0.001 [2]
Current drinker n (%)	97 (33.0)	127 (43.2)	127 (43.2)	200 (68.0)	<0.001 [2]
Hypertension n (%)	77 (26.6)	76 (27.0)	73 (25.7)	70 (24.7)	0.93 [2]
Dietary intake					
Energy (kcal)	1717.4 (426.6)	1578.3 (450.7)	1490.2 (427.8)	1711.2 (470.8)	<0.001 [1]
Protein (g)	77.3 (19.6)	58.4 (17.3)	46.3 (16.5)	37.5 (16.3)	<0.001 [1]
(% energy)	14.8 (2.2)	14.1 (2.4)	13.5 (2.6)	12.5 (2.5)	<0.001 [1]
Fat (g)	47.4 (17.5)	34.9 (14.3)	26.8 (13.0)	20.3 (14.7)	<0.001 [1]
(% energy)	19.9 (4.3)	18.6 (4.6)	17.9 (4.9)	16.9 (5.2)	<0.001 [1]
Carbohydrate (g)	248.6 (87.1)	232.6 (92.4)	233.2 (88.5)	271.5 (111.4)	<0.001 [1]
(% energy)	59.0 (7.1)	60.6 (7.9)	60.9 (8.9)	63.0 (9.4)	<0.001 [1]
Alcohol (g)	1.6 (0, 5.7)	3.3 (0.9, 9.9)	4.0 (2.2, 8.6)	6.2 (1.8, 17.8)	<0.001 [3]
Tea (g)	4.6 (3.4)	4.2 (3.5)	3.5 (2.9)	2.4 (2.7)	<0.001 [1]
Zinc (mg)	9.4 (2.2)	7.7 (2.3)	6.8 (2.2)	6.6 (2.3)	<0.001 [1]
Magnesium (mg)	363.4 (80.9)	292.7 (82.8)	246.3 (83.2)	222.1 (86.9)	<0.001 [1]
Iron (mg)	11.7 (3.1)	8.5 (2.5)	6.3 (2.7)	4.1 (2.7)	<0.001 [1]
β Carotene equivalent (μg)	5960.8 (1836.1)	3731.2 (1574.0)	2129.7 (1477.0)	834.7 (1491.3)	<0.001 [1]
Retinol equivalent (μg)	1529.1 (1983.0)	795.3 (1136.6)	464.6 (880.5)	150.0 (648.1)	<0.001 [1]
Vitamin B1 (mg)	1.3 (0.3)	1.0 (0.3)	0.9 (0.3)	0.8 (0.3)	<0.001 [1]
Vitamin B2 (mg)	1.5 (0.6)	1.1 (0.4)	0.8 (0.4)	0.5 (0.4)	<0.001 [1]
Vitamin B6 (mg)	1.8 (0.3)	1.3 (0.3)	1.0 (0.3)	0.8 (0.3)	<0.001 [1]
Vitamin B12 (mg)	12.6 (7.4)	7.8 (4.8)	5.3 (4.0)	2.5 (3.6)	<0.001 [1]
Vitamin C (mg)	179.5 (51.6)	115.5 (44.7)	75.4 (41.9)	34.4 (45.2)	<0.001 [1]
Vitamin D (μg)	12.2 (5.6)	7.9 (5.5)	4.9 (4.5)	2.1 (4.2)	<0.001 [1]

	DII score				
	Q1	Q2	Q3	Q4	p
Vitamin E (mg)	18.5 (3.5)	15.4 (2.9)	13.6 (3.1)	11.0 (3.7)	<0.001 [1]
Folic acid (μg)	554.3 (207.1)	362.3 (124.6)	242.0 (113.3)	135.9 (109.1)	<0.001 [1]
Niacin (mg)	24.2 (5.8)	19.0 (6.1)	16.1 (5.3)	14.9 (5.7)	<0.001 [1]
SFA (g)	13.2 (6.2)	10.3 (5.6)	8.2 (5.1)	6.6 (5.8)	<0.001 [1]
MUFA (g)	15.5 (6.5)	11.1 (5.1)	8.4 (4.6)	6.3 (5.2)	<0.001 [1]
PUFA (g)	12.0 (4.2)	8.6 (3.3)	6.6 (3.5)	5.0 (3.4)	<0.001 [1]
ω-3 PUFA (g)	2.1 (0.4)	1.7 (0.4)	1.4 (0.3)	1.1 (0.3)	<0.001 [1]
ω-6 PUFA (g)	7.7 (1.5)	6.7 (1.3)	6.1 (1.3)	5.2 (1.5)	<0.001 [1]
Cholesterol (mg)	353.2 (148.2)	259.6 (136.0)	191.1 (134.8)	114.8 (137.8)	<0.001 [1]
Fiber (g)	18.7 (5.0)	13.7 (4.3)	10.7 (4.6)	8.7 (4.6)	<0.001 [1]

DII: dietary inflammatory index, BMI: body mass index, hs-CRP: high-sensitivity C-reactive protein.
DII score, age, body mass index, and dietary intakes, excluding alcohol, are expressed as mean value (standard deviation).
Hs-CRP and alcohol are expressed as median and 25–75th percentiles in parentheses.
Dietary intakes of nutrients and DII excluding energy were adjusted by energy intake using the residual method.
[1] Analysis of variance (ANOVA), [2] Chi-square test, [3] Kruskal-Wallis test, [4] Cochran-armitage trend test.

Table 2 Relation of DII score with serum C-reactive protein levels

	β (95%CI)[1]	*p*
All	0.048 (0.008, 0.087)	0.02
Men	0.085 (0.002, 0.106)	0.04
Women	0.041 (–0.02, 0.103)	0.20

β: regression coefficient.
[1] Adjusted variables were sex, age, smoking habits, drinking habits, history of hypertension, total energy intake, and body mass index.

Table 3 Multivariable adjusted odds ratios for high serum C-reactive protein levels according to DII score

	DII score	OR (95%CI)[1]
All	DII score(quartiles)	
	Q1	1
	Q2	1.05 (0.60, 1.84)
	Q3	1.05 (0.62, 1.77)
	Q4	1.32 (1.01, 2.52)
	DII score (continuous)	1.09 (1.01, 1.19)
Men	DII score (quartiles)	
	Q1	1
	Q2	1.18 (0.72, 1.94)
	Q3	1.26 (0.76, 2.08)
	Q4	1.76 (1.07, 2.92)
	DII score (continuous)	1.10 (1.01, 1.27)
Women	DII score (quartiles)	
	Q1	1
	Q2	0.84 (0.36, 1.95)
	Q3	0.92 (0.43, 1.96)
	Q4	1.09 (0.95, 1.25)
	DII score (continuous)	1.05 (0.52, 2.12)

DII: dietary inflammatory index.

OR(95%CI) : Odds ratio and 95% confidence intervals.

[1] Adjusted variables were sex, age, smoking habits, drinking habits, history of hypertension, total energy intake, and BMI.

DISCUSSION

In this cross-sectional study within the Japan Collaborative Cohort study, we found that a pro-inflammatory diet, as represented as high DII scores, was associated with higher serum hs-CRP concentrations. The results of this study are consistent with the hypothesis that diet modulates inflammation status in the body. Several cross-sectional studies in Western populations[16,29,30] have shown that higher DII scores are associated with high serum hs-CRP concentrations (≥3.0 mg/L). Our results are consistent with these findings in that pro-inflammatory diet, as evidenced by higher DII scores, was associated with increasing circulating hs-CRP concentrations. Even though Japanese have lower serum hs-CRP concentrations than Westerners, the DII scores may be a useful tool for evaluating the total inflammatory potential of diet in Japanese.

It is generally accepted that serum CRP concentrations are higher in men than in women. However, previous studies have not reported on sex differences in the association between the DII score and inflammation markers. In the present study, the DII score was significantly and positively associated with serum hs-CRP concentrations only in men. Results of similar magnitude

were observed in women, but they were not statistically significant. The relatively low number of women with high serum hs-CRP concentrations was the likely explanation for this null finding.

Some studies have reported that overall diets and specific nutrients regulate inflammation. Nanri et al[31] have shown that the healthy dietary pattern (high in vegetables and fruit) is associated with suppressed inflammation using the Japan Multi-Institutional Collaborative Cohort Study (J-MICC Study). Specific nutrients contained in vegetables and fruits, such as vitamin C,[6] fiber,[8] and vitamin E,[32] have consistently been shown to be negatively associated with serum CRP concentrations. On the other hand, intakes of high-fat[33] or high saturated-fat foods[34] have been reported to be associated with increased concentrations of inflammation markers such as IL-6, TNF-α, and CRP. In this study, we observed that subjects with low DII scores tended to have higher intakes of most nutrients, including fat, compared to those with high DII score. These findings are identical to the results of another study using a health examinee cohort.[35] The subjects who consumed high levels of fat also may have consumed more anti-inflammatory/antioxidant foods. This trend implies that the subjects with lower DII scores may have taken various foods to have achieved a nutritionally balanced diet; i.e., without excessive caloric intakes.

The DII score tended to be higher in this study than in previous studies such as the National Health and Nutrition Examination Survey (NHANES)[29] and the SEASONS.[12] Because the method of collecting dietary data is different in each study, the difference in food parameters used for analysis may influence the mean DII score. For calculating DII score, 28 food parameters were used in the NHANES study and 28 food parameters for 7DDR and 44 food parameters for 24HR were available in the SEASONS. Inter-population differences exist on available food parameters. For example, the NHANES study included selenium and caffeine as anti-inflammatory food parameter to perform the DII score calculation; however, we have no data on those parameters in this study. Moreover, some anti-inflammatory food parameters are fairly universal missing including turmeric, flavones, isoflavones, flavonols, ginger, flavan-3-ol, onions, and others. Because these food parameters are typically consumed in small amounts they probably would not have had a large impact on the scoring. Still, the missing information may underestimate the association. The difference between this study and other studies DII scores may be due to those missing food parameters, especially anti-inflammatory food parameters.

There are several limitations in this study. First, serum CRP concentrations of ≥3.0 mg/L is recommended as a relevant clinical cut-off point for identifying individuals at high CVD risk in Westerners.[36] However, Japanese people tend to have lower serum CRP concentrations compared to those of Western people. Among these study subjects, the percentages of those with serum CRP concentrations of ≥3.0 mg/L were 9.7% (n = 63) in men and 6.5% (n = 34) in women. Unlike in Western populations,[12,13] there are too few subjects with serum hs-CRP concentrations of ≥3.0 mg/L to analyze using that value as a clinical cut-off point. We used serum hs-CRP concentrations of 1.0 mg/L as a cut-off point in logistic regression analysis, with reference to the previous study that analyzed hs-CRP and the risk of CHD in a Japanese population.[18] Second, serum hs-CRP concentrations were measured using two different measurement methods (latex-enhanced nephelometry and enzyme-immunoassay). Because the correlation coefficient between enzyme-immunoassay and latex-enhanced nephelometry is very high (r = 0.96), the measurement method did not have a materially relevant effect on the results. Third, the FFQ used in this study provided estimates for only 40 foods and did not include options for food portion size. In general, the fewer parameters available, the higher DII scores; so, the high scores may have been somewhat artefactual.[37] Additionally, energy intake may have been underestimated because some foods simply are not covered by the FFQs. Moreover, there was the non-availability of the remaining 18 food parameters that could be used to calculate the DII score, because only 26 food parameters were available in this study. Comparison of DII scores across studies using

different FFQs should be carefully considered as the available food parameters may be different. Future studies in Japanese populations using more detailed FFQs will be needed to confirm the association between DII score and inflammation markers.

In conclusion, we showed that more pro-inflammatory DII scores were associated with elevated serum hs-CRP concentrations in Japanese subjects with generally lower serum hs-CRP concentrations than their Western counterparts.[12,13] These results, which demonstrate that lower DII scores are associated with higher intakes of nutrients associated with chronic diseases, underline the need for prospective studies to elucidate the causal link between the DII scores and individual inflammatory status in Japanese and other Asian populations that have generally lower levels of chronic, systemic inflammation.

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CONFLICT OF INTEREST

All authors declare no conflicts of interests.

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DISCLOSURE

Dr. James R. Hébert owns controlling interest in Connecting Health Innovations LLC (CHI), a company that has licensed the right to his invention of the dietary inflammatory index (DII®) from the University of South Carolina in order to develop computer and smart phone applications for patient counselling and dietary intervention in clinical settings. Dr. Nitin Shivappa is an employee of CHI.

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