Diet-quality scores and plasma concentrations of markers of inflammation and endothelial dysfunction[1–3]

Teresa T Fung, Marjorie L McCullough, PK Newby, JoAnn E Manson, James B Meigs, Nader Rifai, Walter C Willett, and Frank B Hu

ABSTRACT

Background: Endothelial dysfunction is one of the mechanisms linked to an increased risk of cardiovascular disease.

Objective: We assessed the association between several diet-quality scores and plasma concentrations of markers of inflammation and endothelial dysfunction.

Design: Diet-quality scores on the Healthy Eating Index (HEI), Alternate Healthy Eating Index (AHEI), Diet Quality Index Revised (DQI-R), Recommended Food Score (RFS), and the alternate Mediterranean Diet Index (aMED) were calculated by using a food-frequency questionnaire that was administered in 1990 to 690 women in the Nurses' Health Study (ages 43–69 y, no cardiovascular disease or diabetes). Blood collection was completed in the same year. We used regression analysis to assess the associations between these diet-quality scores and plasma concentrations of C-reactive protein, interleukin 6, E-selectin, soluble intercellular cell adhesion molecule 1, and soluble vascular cell adhesion molecule 1.

Results: The various diet-quality scores were significantly correlated with each other; correlation coefficients ranged from 0.56 to 0.80 (all P values < 0.0001). After adjustment for age, body mass index, alcohol intake, physical activity, smoking status, and energy intake, the HEI and DQI-R were not significantly associated with any of the biomarkers, whereas the AHEI and aMED scores were associated with significantly lower concentrations of most biomarkers. The RFS was significantly associated with a lower concentration of E-selectin only. C-reactive protein concentrations were 30% ($P < 0.05$) and 24% ($P < 0.05$) lower in the top than in the bottom quintile of the AHEI and of the aMED, respectively

Conclusion: Higher AHEI and aMED scores were associated with lower concentrations of biomarkers of inflammation and endothelial dysfunction and therefore may be useful as guidelines for reducing the risk of diseases involving such biological pathways. *Am J Clin Nutr* 2005;82:163–73.

KEY WORDS Diet, diet quality, inflammation, endothelial dysfunction, women

INTRODUCTION

Endothelial dysfunction and inflammation are believed to be involved in diseases such as atherosclerosis and diabetes (1, 2). High concentrations of markers of inflammation and endothelial dysfunction, such as C-reactive protein (CRP), interleukin 6 (IL-6), E-selectin, and soluble intercellular adhesion molecule 1 (sICAM-1), have been shown to predict cardiovascular disease risk (3–5). Data are also emerging about their involvement in the development of diabetes. A recent study showed a positive association between serum concentrations of sICAM-1 and E-selectin and risk of diabetes (6). The associations between foods, nutrients, and these diseases may be mediated in part through inflammation and endothelial dysfunction. Studies have suggested a link between dietary intake of long-chain n−3 fatty acids and antioxidants and endothelial dysfunction (7) and of alcohol (8), vitamin B-6 intake, and glycemic index (9) and plasma CRP concentrations (10). However, data are scant on the association between overall dietary patterns and these biomarkers.

Several indexes to assess overall diet quality have been proposed. The Healthy Eating Index (HEI) developed by the US Department of Agriculture was based on the *Dietary Guidelines for Americans* and the *Food Guide Pyramid* (11). The *Diet Quality Index Revised* (DQI-R) is based on similar guidelines from the National Research Council but also includes iron and calcium (12). The Recommended Food Score (RFS) was constructed from foods recommended from the current intake guidelines (13). Our group previously revised the HEI according to the most recent scientific evidence to focus on the healthier items in the food guide pyramid food groups (14). This Alternate Healthy Eating Index (AHEI) was found to be better than the original HEI or RFS at predicting the risk of cardiovascular disease and the overall incidence of major chronic diseases. Mortality and rates

[1] From the Department of Nutrition, Simmons College, Boston, MA (TTF); the Department of Nutrition, Harvard School of Public Health, Boston, MA (TTF, WCW, and FBH); Epidemiology and Surveillance Research, American Cancer Society, Atlanta, GA (MLM); the Jean Mayer US Department of Agriculture Human Nutrition Research Center on Aging, Tufts University, Boston, MA (PKN); the Department of Medicine, Channing Laboratory, Brigham and Women's Hospital and Harvard Medical School, Boston, MA (JEM, WCW, and FBH); the Department of Epidemiology, Harvard School of Public Health, Boston, MA (JEM, WCW, and FBH); the Department of Laboratory Medicine, Children's Hospital, Boston, MA (NF); and the Department of Medicine, Massachusetts General Hospital, Boston, MA (JEM).

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[3] Reprints not available. Address correspondence to TT Fung, Department of Nutrition, Simmons College, 300 The Fenway, Boston, MA 02115. E-mail: fung@simmons.edu.

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of several chronic diseases are lower in the Mediterranean region, and the traditional regional diet is believed to play a role in this lower risk (15). Trichopoulou et al (16) developed a scale to quantify this diet in the Greek population. We adapted this to develop the alternate Mediterranean Diet Score (aMED) to use with a food-frequency questionnaire (FFQ) developed in the United States.

Because the purpose of these diet-quality indexes is to assess and guide an individual's dietary intake for the promotion of health and prevention of disease, they need to be examined for their utility. One approach is to assess and compare how well these measures of diet quality relate to biomarkers of disease risk or disease endpoints. In this analysis, we focused on the relation between these diet-quality indexes and biomarkers of inflammation and endothelial dysfunction. Specifically, we assessed the associations between the HEI score, an alternate HEI score, the RFS, the DQI-R, and the aMED and plasma concentrations of C-reactive protein (CRP), interleukin 6 (IL-6), E-selectin, soluble intercellular adhesion molecule 1 (sICAM-1), and soluble vascular cell adhesion molecule 1 (sVCAM-1).

SUBJECTS AND METHODS

Subjects

The Nurses' Health Study was established in 1976 with the enrollment of 121 700 female nurses in the United States. The study was approved by the Institutional Review Board of the Brigham and Women's Hospital, Boston, MA. Every 2 y, questionnaires were sent to update health, medical, and lifestyle information. A validated, semiquantitative FFQ was sent every 4 y to collect information on dietary intake for the previous year. In this study, we included 690 nurses who were selected as control subjects in a previous nested case-control study of diabetes. These women were 43–69 y of age and had no history of cardiovascular disease, cancer, or diabetes at the time blood was drawn.

Blood collection and measurement of biomarkers

Blood was collected in 1989–1990. Each willing participant was sent a blood collection kit containing instructions and needed supplies (eg, blood tubes and needles). Each participant made arrangements for blood to be drawn, packaged the sample in an enclosed cool pack, and sent it to the laboratory by overnight courier. Almost all of the samples arrived within 26 h after blood was drawn. On arrival at the laboratory, the whole-blood samples were centrifuged (1200 × *g*, 15 min, room temperature) separated into aliquots, and stored at temperatures no higher than −80 °C. The lifestyles and dietary intakes of women who returned a blood sample were in general similar to those who did not provide a blood sample. All biomarkers were measured in the Clinical Chemistry Laboratory at the Children's Hospital in Boston. CRP was measured with a latex-enhanced turbidimetric assay on a Hitachi 911 (Denka Seiken, Tokyo, Japan). IL-6 was measured with an ultrasensitive enzyme-linked immunosorbent assay (R&D Systems, Minneapolis, MN). E-selectin, sICAM-1, and sVCAM-1 were measured with a commercial enzyme-linked immunosorbent assay (R&D Systems). Interassay CVs were 3.4–3.8% for CRP, 5.8–8.2% for IL-6, 6.4–6.6% for E-selectin, 6.1–10.1% for sICAM-1, and 8.5–10.2% for sVCAM-1.

Assessment of dietary intake and diet-quality scores

The 1990 FFQ included ≈140 food items. A standard portion size was given for each food item. Cohort members were asked to choose from 9 possible frequency responses ranging from "never" to ">6 times/d" for each food. Previous validation studies among members of the Nurses' Health Study cohort showed good correlations between nutrients assessed with the FFQ and with multiple weeks of food records completed over the previous year (17, 18). Intake information from the FFQ was used to calculate the various diet-quality scores.

Calculation of the HEI was based on criteria set in *The Healthy Eating Index Final Report* (11) and adapted to this cohort by McCullough et al (19) (*see* **Appendix A**). Briefly, the HEI contains 10 components that reflect recommendations based on the *Food Guide Pyramid* (20) and the *Dietary Guidelines for Americans* (21). Recipe ingredients for mixed items were allocated to the appropriate food groups. Possible scores from each component ranged from 0 to 10, depending on level of intake, with a total possible score of 100 for the HEI. The AHEI scoring criteria (14) differ from those of the original HEI; more specific items, such as protein source, *trans* fat, ratio of polyunsaturated to saturated fat, and cereal fiber, are used in the AHEI rather than the broader terms, such as grains, total fats, and all meats combined, used in the HEI (*see* Appendix A). In addition, points were awarded for moderate alcohol consumption and long-term multivitamin use. The possible score for the multivitamin component was either 2.5 or 7.5 to avoid overweighting. The AHEI was based on 9 items, with a maximum possible score of 87.5.

The RFS was developed by Kant et al (13, 22) and adapted by McCullough et al (14) for our FFQ. The RFS focused on fruit, vegetables, whole grains, lean meats or meat alternates, and low-fat dairy products. Participants received 1 point for each recommended food consumed at least weekly. Based on the length of our FFQ, the maximum possible score was 51 (*see* Appendix A)

The DQI-R score was based on methods by Haines et al (12) and adapted for our FFQ by Newby et al (23) Briefly, the DQI-R consists of 10 components that measure intake of several food groups and nutrients and diet diversity and moderation. The range of possible scores for each component is 0–10 points, depending on the level of intake, and the maximum possible DQI-R score is 100 points.

The aMED score was based on the Mediterranean diet scale of Trichopoulou et al (16, 24) The original score was based on the intake of 9 items: vegetables, legumes, fruit and nuts, dairy, cereals, meat and meat products, fish, alcohol, and the ratio of monounsaturated to saturated fat. Intakes above the median of the study subjects received 1 point; all other intakes received 0 points. Meat and dairy product consumption less than the median received 1 point. We modified the original scale for this study by excluding potato products from the vegetable group, separating fruit and nuts into 2 groups, eliminating the dairy group, including whole-grain products only, including only red and processed meats for the meat group, and assigning alcohol intake between 5 and 15 g/d for 1 point. These modifications were based on dietary patterns and eating behaviors that have been consistently associated with lower risks of chronic disease in clinical and epidemiologic studies. Possible scores on the aMED ranged from 0 to 9 (*see* Appendix A).

TABLE 1
Age-standardized lifestyle characteristics by quintile (Q) of diet-quality scores[1]

Quintile of diet score[2]	BMI	Current smoker	Activity[3]	Energy intake	Total fat	Fiber	Glycemic load
Healthy Eating Index		%	*MET h/wk*	*kcal/d*	*g/d*	*g/d*	
Q1 (36.0–66.4)	26.6 ± 6.8	27 ± 44	10 ± 13	1495 ± 626	62 ± 33	12.9 ± 5.2	121 ± 54
Q3 (74.6–80.5)	27.0 ± 5.9	18 ± 38	14 ± 15	1713 ± 518	60 ± 25	19.3 ± 8.0	160 ± 55
Q5 (86.6–98.7)	25.1 ± 5.2	5 ± 22	17 ± 19	2053 ± 379	63 ± 16	26.1 ± 7.7	212 ± 50
P for trend	0.05	<0.0001	0.0005	<0.0001	0.55	<0.0001	<0.0001
Alternate Healthy Eating Index							
Q1 (15.7–32.3)	27.5 ± 6.9	24 ± 43	10 ± 13	1559 ± 513	61 ± 26	13.4 ± 4.4	138 ± 51
Q3 (38.9–44.6)	25.7 ± 5.3	10 ± 30	13 ± 16	1848 ± 532	66 ± 26	19.7 ± 5.7	171 ± 53
Q5 (51.8–78.5)	25.1 ± 5.2	4 ± 19	16 ± 19	1975 ± 494	63 ± 22	27.7 ± 9.1	197 ± 64
P for trend	0.03	<0.0001	0.004	<0.0001	0.09	<0.0001	<0.0001
Diet Quality Index Revised							
Q1 (32.1–54.7)	26.8 ± 6.7	28 ± 45	9 ± 11	1608 ± 587	68 ± 30	13.7 ± 5.0	131 ± 52
Q3 (63.0–70.4)	27.0 ± 6.4	8 ± 28	14 ± 14	1799 ± 506	65 ± 24	19.6 ± 6.5	163 ± 52
Q5 (80.4–93.9)	25.2 ± 5.1	6 ± 23	16 ± 15	1901 ± 432	54 ± 16	26.3 ± 9.4	207 ± 62
P for trend	0.006	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001
Recommended Food Score							
Q1 (1–12)	26.2 ± 6.2	22 ± 42	9 ± 11	1536 ± 560	58 ± 28	13.0 ± 4.6	138 ± 61
Q3 (17–19)	26.1 ± 6.4	11 ± 32	14 ± 14	1792 ± 499	63 ± 22	20.0 ± 6.1	168 ± 59
Q5 (25–41)	27.0 ± 6.7	6 ± 24	15 ± 18	2099 ± 453	68 ± 23	27.4 ± 8.6	208 ± 55
P for trend	0.41	<0.0001	<0.0001	<0.0001	0.0005	<0.0001	<0.0001
Alternate Mediterranean Diet Index							
Q1 (0–2)	27.1 ± 6.8	23 ± 42	9 ± 10	1533 ± 486	56 ± 22	13.2 ± 4.0	138 ± 52
Q3 (4)	26.3 ± 5.8	11 ± 32	15 ± 16	1742 ± 457	63 ± 23	19.2 ± 5.6	161 ± 52
Q5 (5)	26.5 ± 6.1	10 ± 29	15 ± 17	2033 ± 492	68 ± 24	26.8 ± 8.5	200 ± 58
P for trend	0.43	0.001	0.004	<0.0001	<0.0001	<0.0001	<0.0001

[1] All values are $\bar{x}$ ± SD; n = 660.
[2] Range in parentheses.
[3] Walking and flights of stairs climbed; expressed as metabolic equivalent (MET) hours per week.

Assessment of other variables

Smoking status was self-reported in the 1990 main questionnaire. Body mass index (BMI) was calculated from the height reported in 1976 and the weight reported in 1990. Physical activity was expressed as hours of walking and flights of stairs climbed per week in 1990 and was converted to metabolic equivalent (METs) hours per week.

Statistical analysis

We calculated z scores for each of the diet-quality scores; log-transformation did not influence the results, so nontransformed data are presented. We then used a multivariate linear regression with a robust variance estimate (25) to examine associations between 1-z score increases in diet-quality score and biomarker concentrations. This variance estimator allows for valid inference without the assumption of normal distribution in the dependent variable. The regression models were adjusted for age (continuous), alcohol intake (nondrinker, 0.1–4.9 g, 5.0–9.9 g, ≥10 g/d), smoking status (never smokers, past smokers, current smokers of ≤14 cigarettes/d, and current smokers of >14 cigarettes/d), physical activity (<1.5, 1.5–5.9, 6–11.9, 12–20.9, ≥21 METs/wk), total energy intake (quintiles), and BMI (continuous). In addition, we also compared the geometric means of biomarker concentrations between women at the top and bottom quintiles for each diet-quality score. Then we compared this difference with t tests, including Bonferroni correction, between different diet-quality score.

RESULTS

The mean (±SD) diet-quality scores of our 660 participants were as follows: HEI = 77 ± 11, AHEI = 43 ± 11, DQI-R = 68 ± 13, RFS = 18 ± 7, and aMED = 4.4 ± 1.8. Mean (±SD) biomarker values were as follows: CRP = 2.8 ± 3.5 mg/L, IL-6 = 2.4 ± 3.8 ng/L, E-selectin = 48.8 ± 23.6 ng/L, sICAM-1 = 257 ± 78 μg/L, and sVCAM-1 = 547 ± 165 μg/L. The age-standardized lifestyle characteristics of the participants are shown in **Table 1**. Lower BMI was noted with higher scores of HEI, AHEI, and DQI-R. On all diet-quality indexes, individuals who scored high were less likely to be smokers and had higher levels of physical activity. Because a greater food intake may result in meeting consumption criteria of food items specified in various diet-quality scores, we observed that a higher

TABLE 2
Spearman's correlation coefficients among diet-quality scores from the 1990 food-frequency questionnaire[1]

	AHEI	DQI-R	RFS	aMED
HEI	0.60	0.80	0.69	0.60
AHEI	1.00	0.64	0.56	0.75
DQI-R		1.00	0.57	0.59
RFS			1.00	0.65

[1] n = 660. HEI, Healthy Eating Index; AHEI, Alternate Healthy Eating Index; DQI-R, Diet Quality Index Revised; RFS, Recommended Food Score; aMED, alternate Mediterranean Diet Index. All P values are < 0.0001.

TABLE 3
Unadjusted mean biomarker values according to quintile (Q) of diet-quality scores[1]

	CRP (mg/L)				IL-6 (ng/L)				E-selectin (ng/L)				sICAM-1 (μg/L)				sVCAM-1 (μ/L)			
	Q1	Q3	Q5	*P* for trend	Q1	Q3	Q5	*P* for trend	Q1	Q3	Q5	*P* for trend	Q1	Q3	Q5	*P* for trend	Q1	Q3	Q5	*P* for trend
HEI	2.0 ± 10.1	2.7 ± 2.8	1.7 ± 9.1	0.01	2.8 ± 3.4	2.2 ± 1.6	2.3 ± 2.2	0.03	51.4 ± 25.9	47.2 ± 16.6	44.8 ± 18.3	0.0007	263 ± 103	256 ± 60	25.1 ± 44	0.005	531 ± 243	527 ± 122	533 ± 123	0.46
	(36.0–66.4)	(74.6–80.5)	(86.6–98.7)		(36.0–66.4)	(74.6–80.5)	(86.6–98.7)		(36.0–66.4)	(74.6–80.5)	(86.6–98.7)		(36.0–66.4)	(74.6–80.5)	(86.6–98.7)		(36.0–66.4)	(74.6–80.5)	(86.6–98.7)	
AHEI	3.8 ± 4.5	1.1 ± 13.5	2.1 ± 2.4	<0.0001	3.5 ± 3.8	2.3 ± 1.8	2.0 ± 1.2	0.0006	60.7 ± 30.2	47.8 ± 24.7	42.5 ± 16.3	<0.0001	286 ± 108	250 ± 69	247 ± 45	0.0004	607 ± 270	524 ± 133	544 ± 126	0.02
	(15.7–32.3)	(38.9–44.6)	(51.8–78.5)		(15.7–32.3)	(38.9–44.6)	(51.8–78.5)		(15.7–32.3)	(38.9–44.6)	(51.8–78.5)		(15.7–32.3)	(38.9–44.6)	(51.8–78.5)		(15.7–32.3)	(38.9–44.6)	(51.8–78.5)	
DQIR	2.4 ± 10.4	2.2 ± 9.7	1.7 ± 9.0	0.005	2.7 ± 2.8	2.4 ± 2.1	2.2 ± 1.3	0.01	54.3 ± 29.0	51.3 ± 30.7	45.1 ± 19.2	0.0004	276 ± 104	260 ± 112	255 ± 51	0.03	567 ± 255	544 ± 151	544 ± 134	0.31
	(32.1–54.7)	(63.0–70.4)	(80.4–93.9)		(32.1–54.7)	(63.0–70.4)	(80.4–93.9)		(32.1–54.7)	(63.0–70.4)	(80.4–93.9)		(32.1–54.7)	(63.0–70.4)	(80.4–93.9)		(32.1–54.7)	(63.0–70.4)	(80.4–93.9)	
RFS	2.0 ± 9.6	2.9 ± 4.0	1.6 ± 9.8	0.29	2.8 ± 3.3	2.5 ± 2.8	2.4 ± 2.3	0.19	52.5 ± 23.7	48.4 ± 32.2	46.2 ± 25.5	0.01	261 ± 66	271 ± 137	243 ± 62	0.03	548 ± 163	551 ± 245	529 ± 121	0.41
	(1–12)	(17–19)	(25–41)		(1–12)	(17–19)	(25–41)		(1–12)	(17–19)	(25–41)		(1–12)	(17–19)	(25–41)		(1–12)	(17–19)	(25–41)	
aMED	3.4 ± 4.0	1.3 ± 13.4	2.5 ± 2.8	0.002	2.9 ± 3.5	2.3 ± 1.7	2.1 ± 1.6	0.004	54.8 ± 32.4	48.1 ± 17.0	44.9 ± 23.4	0.0006	282 ± 134	246 ± 48	254 ± 59	0.02	578 ± 238	527 ± 137	539 ± 121	0.06
	(0–2)	(4)	(5)		(0–2)	(4)	(5)		(0–2)	(4)	(5)		(0–2)	(4)	(5)		(0–2)	(4)	(5)	

[1] All values are $\bar{x}$ ± SE; range in parentheses. $n = 660$. HEI, Healthy Eating Index; AHEI, Alternate Healthy Eating Index; DQI-R, Diet Quality Index Revised; RFS, Recommended Food Score; aMED, alternate Mediterranean Diet Index; sICAM-1, soluble intercellular cell adhesion molecule 1; sVCAM-1, soluble vascular cell adhesion molecule 1; CRP, C-reactive protein; IL-6, interleukin 6.

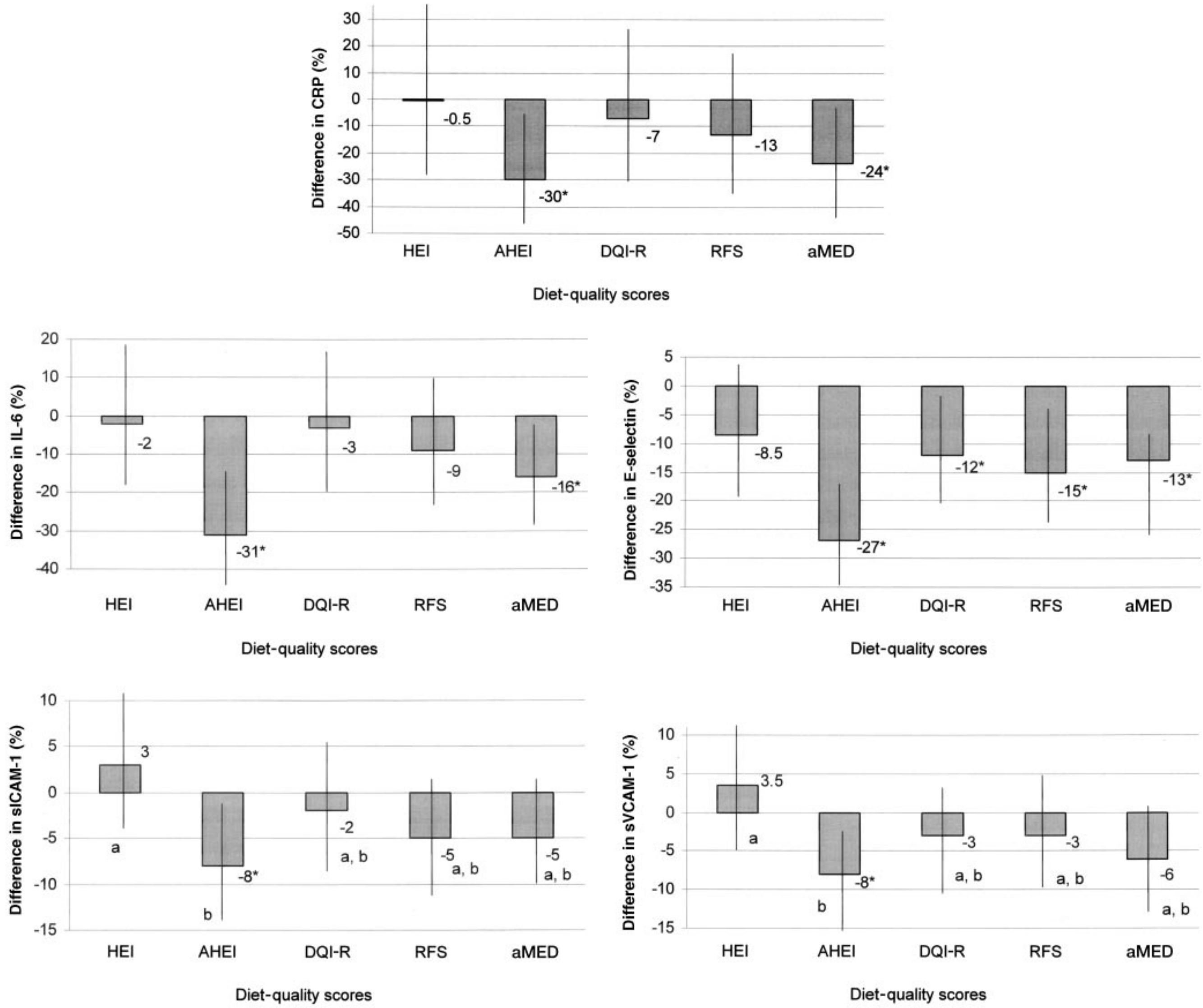

FIGURE 1. Geometric mean percentage differences in the biomarkers C-reactive protein (CRP), interleukin 6 (IL-6), E-selectin, soluble intercellular cell adhesion molecule 1 (sICAM-1), and soluble vascular cell adhesion molecule 1 (sVCAM-1) by diet-quality score. Comparisons were made between the 5th and 1st quintiles. Values were adjusted for age, alcohol intake, smoking status, physical activity, total energy intake, and BMI. HEI, Healthy Eating Index [$n = 117$ for quintile (Q) 1 and 142 for Q5]; AHEI, Alternate Healthy Eating Index ($n = 108$ for Q1 and 134 for Q5); DQI-R, Diet Quality Index Revised ($n = 115$ for Q1 and 141 for Q5); RFS, Recommended Food Score ($n = 128$ for Q1 and 119 for Q5); aMED, alternate Mediterranean Diet Score ($n = 135$ for Q1 and 168 for Q5). Note that the *y* axes are not the same in all panels. Vertical lines represent 95% CIs. Bars with different lowercase letters are significantly different, $P < 0.05$ (Bonferroni-corrected Student's *t* tests). *The difference between the 5th and 1st quintiles was significantly different, $P < 0.05$ (linear regression).

score in general represented higher energy intakes. Correlations between the diet-quality scores were relatively high because many of the scores were based on similar dietary recommendations (**Table 2**). The highest correlation, $r = 0.80$ ($P < 0.0001$), was between the HEI and DQI-R. The actual values of the biomarkers at the top, middle, and bottom quintiles of each diet-quality score are shown in **Table 3**. Differences in biomarker values between extreme quintiles of diet-quality scores were the greatest for the AHEI and aMED (**Figure 1**). We compared biomarker differences between the 5th and 1st quintiles for the different diet-quality scores. The only significant difference was between HEI and AHEI for sICAM-1 and sVCAM-1.

After age, BMI, smoking status, physical activity, and energy and alcohol intakes were adjusted for, we found that the HEI, DQI-R, and RFS were, in general, not significantly associated with biomarker concentrations (**Table 4**). However, each 1-*z* score increase on the AHEI and aMED was associated with significantly lower concentrations of many of these biomarkers. Of all the diet-quality scores, AHEI appeared to have the strongest associations with biomarker concentrations; the differences between the 5th and 1st quintiles of the AHEI scores ranged from 8% for concentrations of sICAM-1 and sVCAM-1 to 31% for concentrations of IL-6 (Figure 1). Higher aMED scores were also associated with a more favorable biomarker profile. Comparing top to bottom quintiles of aMED score, we found a reduction in biomarker concentrations of 24% in CRP, 16% in IL-6, and 13% in e-selectin concentrations. After additional adjustment for BMI, DQI-R scores were not associated with any biomarker concentrations (Table 4), and HEI and RFS scores were associated with a lower concentration of E-selectin only. Our results

TABLE 4
β Coefficients for a 1-z score increase in diet-quality scores[1]

Score	CRP (mg/L)	IL-6 (ng/L)	E-selectin (ng/L)	sICAM-1 (μg/L)	sVCAM-1 (μg/L)
HEI					
Age and energy adjusted	−0.44[2]	−0.33[2]	−4.49[3]	−12.92[2]	−8.08
MV adjusted	−0.32[4]	−0.22	−3.03[2]	−5.50	−5.35
MV + BMI adjusted	−0.04	−0.20	−1.93	−3.86	−2.17
AHEI					
Age and energy adjusted	−0.65[3]	−0.40[2]	−6.31[3]	−14.47[2]	−14.39[4]
MV adjusted	−0.60[3]	−0.33[2]	−5.57[3]	−8.15[4]	−13.85
MV + BMI adjusted	−0.36[2]	−0.30[2]	−4.74[3]	−6.93[4]	−11.04
DQI-R					
Age and energy adjusted	−0.48[3]	−0.24[2]	−4.26[3]	−9.73[2]	−11.42
MV adjusted	−0.38[2]	−0.14	−2.94[2]	−2.83	−10.15
MV + BMI adjusted	−0.07	−0.11	−1.70	−1.30	−6.82
RFS					
Age and energy adjusted	−0.22	−0.17	−3.70[3]	−5.51[2]	−7.39
MV adjusted	−0.10	−0.08	−2.39[4]	−2.53	−5.12
MV + BMI adjusted	0.05	−0.11	−2.38[4]	−2.25	−3.57
aMED					
Age and energy adjusted	−0.57[3]	−0.37[2]	−4.63[3]	−11.35[2]	−15.57[4]
MV adjusted	−0.50[2]	−0.31[2]	−3.90[2]	−7.38[4]	−14.99[4]
MV + BMI adjusted	−0.36[2]	−0.29[2]	−3.48[2]	−6.84	−13.07[4]

[1] $n = 660$. MV, multivariate linear regression adjusted for age, alcohol intake, smoking status, physical activity, and total energy intake; HEI, Healthy Eating Index; AHEI, Alternate Healthy Eating Index; DQI-R, Diet Quality Index Revised; RFS, Recommended Food Score; aMED, alternate Mediterranean Diet Index; sICAM-1, soluble intercellular cell adhesion molecule 1; sVCAM-1, soluble vascular cell adhesion molecule 1; CRP, C-reactive protein; IL-6, interleukin 6.

[2] $P < 0.01$.

[3] $P < 0.0001$.

[4] $P < 0.05$.

remained essentially the same when alcohol intake was not included in the regression models.

DISCUSSION

We compared the associations between the different diet-quality scores and biomarkers of inflammation and endothelial dysfunction. We found that the AHEI and aMED scores had the strongest inverse associations with these biomarkers and that the HEI, DQI-R, and RFS scores had little association with these biomarkers.

Differences in associations between indexes and biomarkers of inflammation and endothelial dysfunction are likely attributable to differences in the food and nutrient components of each index. For example, both the AHEI and aMED scores focus on dietary patterns high in fruit and vegetables, whole grains, nuts, and fish and moderate in alcohol, and these 2 scores were highly correlated in our sample. The AHEI further awards points to diets with a high ratio of polyunsaturated to saturated fat, whereas the aMed score also awards points for diets with a high ratio of monounsaturated to saturated fat. Therefore, these 2 scoring systems are unique in that they can capture diets high in long-chain n−3 fatty acids. Previous studies have shown an association between the intake of long-chain n−3 fatty acids and lower concentrations of inflammatory markers (7). Recent studies have continued to show favorable changes in CRP, IL-6, and sVCAM-1 with supplementation with α-linolenic acid or oils rich in long-chain n−3 fatty acids (26–28). On the other hand, diets high in *trans* fat or saturated fat were found to be associated with higher concentrations of CRP, IL-6, and E-selection in a 5-wk randomized crossover study in men (29). In another randomized trial, a diet low in saturated fat and high-fat dairy products but high in refined grains was effective at lowering CRP concentrations but was not as effective as were lovastatin and a diet high in plant sterols, soy protein, viscous fiber, and almonds (30).

The lack of association of RFS, DQI-R, and HEI with biomarkers of inflammation and endothelial dysfunction may be explained by the nonspecificity of fat and carbohydrate quality, emphasis on lower total fat intake, and broad inclusion of many foods in these indexes. The HEI is based on the food guide pyramid, which gives more points for a diet low in all types of fat, including unsaturated fats. It also allows individuals to score higher points if their diet contains refined grains. The scoring criteria also included sodium intake and diet variety. Although meaningful for an overall healthy diet, these components are not specific to inflammation. The DQI-R is similar to the HEI, and these 2 scores were highly correlated in the present study. However, the DQI-R also includes calcium and iron intakes, which again, may not be related to inflammation. The RFS criteria include intakes of vegetables, fruit, healthy protein sources, grains, and dairy products but it also does not distinguish between different types of fatty acids or penalize for consumption of items that are not recommended. The AHEI, but not the HEI and RFS, has been shown to predict cardiovascular disease risk in women (14, 19). High scores on the HEI, DQI-R, and RFS do not capture differences in types of fats, which probably contributed to the poor performance of these indexes in the present study. Therefore, although these indexes may reflect certain aspects of diet quality, they may be poor choices for evaluating diet quality specifically for reducing the risk of diseases influenced by inflammation, such as cardiovascular disease and diabetes.

In our analysis, the HEI and DQI-R scores were somewhat higher than those obtained in the US Continuing Survey of Food Intakes by Individuals 1994–1996 (12, 19): 77 compared with 64 and 68 compared with 63, respectively. However, in our sample, the mean score of the 1st quintile was 59 with both the HEI and the DQI-R, and the mean score of the 5th quintile was 91 with the HEI and 86 with the DQI-R. Therefore, we still had a substantial contrast in the distribution of diet-quality scores in our sample to detect any association with biomarkers.

In our analysis, the AHEI was the strongest correlate for IL-6, which decreased by 0.30 ng/L for each 1–*z* score increase on the AHEI (Table 4). This finding is comparable with the difference between obese and normal-weight (3.18 compared with 1.4 pg/mL) premenopausal women and in obese women after a weight loss of ≥10% (31). In a comparison of the top- and bottom-quintile AHEI scores, the reduction in sICAM-1 and sVCAM-1 in our sample (8%) was similar to that for obese women who sustained a weight loss of ≥10% (31). Because we adjusted our analysis for BMI and only studied women free of disease, our study results suggest that the AHEI is capable of capturing associations between diet and markers of inflammation even in healthy-weight individuals, independent of adiposity.

This analysis was controlled extensively for potential lifestyle predictors of biomarkers; therefore, any confounding would be minimal. However, because of the cross-sectional nature of this study, we cannot infer causality from our results. Diet-quality indexes comprise a combination of many food groups or food components. Components of each of the indexes could have different influences on biomarkers. In addition, diet-quality indexes or their components may influence more than one pathway of endothelial dysfunction and inflammation. The diet-quality indexes that we examined were based on North American dietary habits. It is important to examine dietary patterns in other populations (eg, Asian and Mediterranean) and their relations with biomarkers for the development of chronic diseases.

In conclusion, we found that dietary indexes that reflect current intake guidelines were not predictive of biomarkers of inflammation and endothelial dysfunction. In contrast, the AHEI and aMED scores were strongly associated with lower concentrations of biomarkers of inflammation and endothelial dysfunction. Because these pathologic processes are linked to the development of cardiovascular disease and diabetes, our data suggest a possible mechanism for the role of diet quality in relation to the risk of diabetes and cardiovascular disease. Therefore, these 2 diet-quality indexes may be useful as guidelines for reducing the risk of diseases.

TTF designed and conducted the analysis and drafted the manuscript. PKN and MLM assisted with the statistical analysis. JEM, WCW, FBH, and TTF secured funding for the project. NR analyzed the blood samples. All authors participated in the revision and approval of the manuscript. None of the authors had a conflict of interest.

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APPENDIX A

Scoring criteria for diet-quality indexes

Healthy Eating Index (1)[1]

		Criteria[2]		
Component	Foods included	<50 y	≥51 y	Score
Grains	Cooked and cold cereals, loaf breads and quick breads, rice, pasta, pizza, pancakes, pies, crackers, cookies, other grains, brownies, donuts, cakes, sweet rolls, bran, wheat germ, chowder	9.1 servings/d	7.4 servings/d	10; 1 point less for each 10% less than intake required for full score
Vegetables	All vegetables, potato products, pizza, chowder, tomato products	4.2 servings/d	3.5 servings/d	Same as above
Fruit	Fruit, fruit juices, pies	3.2 servings/d	2.5 servings/d	Same as above
Milk	Milk, sherbet, ice cream, yogurt, cheeses, pizza, potatoes, chocolate, chocolate candies, chowder	2.0 servings/d	2.0 servings/d	Same as above
Meat	Eggs, chicken, processed meats, red meats, seafood, tofu, soymilk, tree nuts, peanuts, peanut butter, chocolate, brownie, organ meats, beans, chowder	2.4 servings/d	2.2 servings/d	Same as above
Total fat		≤30% of energy	≤30 of energy	10
		31–44 of energy	31–44 of energy	5
		≥45 of energy	≥45 of energy	0
Saturated fat		≤10% of energy	≤10% of energy	10
		11–14% of energy	11–14% of energy	5
		≥15% of energy	≥15% of energy	0
Cholesterol		<300 mg	<300 mg	10
		301–449 mg	301–449 mg	5
		≥450 mg	≥450 mg	0
Sodium		≤2400 mg	≤2400 mg	10; 1 point less for each 10% less than intake required for full score
Variety		Top 10% intake of the sum of unique foods	Top 10% intake of the sum of unique foods	Same as above

[1] The amount of food in each food groups (eg, the amount of milk in chowder) was adjusted according to a recipe so that food with small amounts of the food group would not contribute excessively to that food group.

[2] Based on 2200 kcal for the < 50 y category and 1900 kcal for the ≥ 51 y category.

Alternate Healthy Eating Index (2)

Component	Foods included	Criteria	Score
Vegetables	All vegetables, tomato products, yams, pizza (does not include potatoes)	5 servings/d	10; 1 point less for each 10% less than intake required for full score
Fruit	All fruit and fruit juices	4 servings/d	Same as above
Nuts and soy	Tree nuts, peanuts, peanut butter, tofu, soymilk	1 servings/d	Same as above
Ratio of white to red meat	White: chicken, seafood; red: processed meats, red meats, organ meats	4	Same as above
Cereal fiber	—	15 g/d	Same as above
trans Fat	—	≤0.5% of energy	10
		>0.5 but <4.0% of energy	1 point less for each 10% increment in this range
	—	≥4	0
Ratio of polyunsaturated to saturated fat		≥1	10; 1 point less for each 10% less than intake required for full score
Long-term multivitamin use	—	≥5 y	7.5 points for ≥5 y regular use; 2.5 for all others
Alcohol	Red and white wine, beer, "light" beer, liquor	Men: 1.5–2.5 servings/d; women: 0.5–1.5 servings/d	10
		Intake < "ideal"	1 point less for each 10% less than ideal intake
		Intake > "ideal"	1 point less for each 10% above than ideal intake
		Men: 0 or > 3.5 servings/d; women: 0 or >2.5 servings/d	0
			0

Diet Quality Index Revised (3)[1]

Component	Foods included	Criteria[2] <50 y	Criteria[2] ≥51 y	Score
Grains	Crackers, cereals, pizza, dark breads, rice, bran, wheat germ, breads, oatmeal, pasta, English muffins, muffins, pancakes, other grains	≥9 servings/d	≥7.4 servings/d	10; 1 point less for each 10% less than intake required for full score
Vegetables	All vegetables, yams, potatoes, French fries, corn, tomato juice, tomato sauce, tofu, legumes, tofu	≥4 servings/d	≥3.5 servings/d	Same as above
Fruit	All fruit and juices (except tomato juice)	≥3 servings/d	≥2.5 servings/d	Same as above
Total fat		≤30% of energy	Same as for <50 y	10
		30.1–40% of energy		5
		>40% of energy		0
Saturated fat		≤10% of energy	Same as for <50 y	10
		10.1–13% of energy		5
		>13% of energy		0
Cholesterol		≤300 mg	Same as for <50 y	10
		301–400 mg		5
		>400 mg		0
Calcium (AI for age)		1000 mg	1200 mg	10; 1 point less for each 10% less than intake required for full score
Iron (RDA for age)	—	18 mg	8 mg	Same as above
Diet diversity (based on sum of 4 categories)	Grains: non-whole-grain breads, quick breads, whole-grain breads, pasta, cereals, rice, other grains	≥0.25 servings/d of each food = 1 point; the total for each category is averaged by the number of foods in the category (eg, 3 for fruit) and then multiplied by 2.5	Same as for < 50 y	Maximum of 2.5 points for each category; maximum of 10; total diversity = grains + vegetables + fruit + protein
	Vegetables: yellow and orange, deep green (spinach, broccoli); tomato products, beans, tofu, soy, starchy vegetables, other vegetables			
	Fruit: citrus, berry, melon, juices, other fruit			
	Protein: beef, pork, organ meat, deli meat, chicken, milk, cheese, eggs, soups, seafood, yogurt			
Diet moderation	Amount of added fat from cream, butter, margarine, cream cheese, oil and vinegar dressing, chocolate, whole milk, sour cream, ice cream, mayonnaise and creamy dressings, other cheese, cookies, chowder and cream soups, sherbet, French fries, brownies, muffins and biscuits, donuts, pancakes and waffles, cakes, pies, sweet rolls, coffee cake, pastries	Added fat: <2.5 g/d 25.1–50 g 50.1–75 g >75 g	Same as for < 50 y	 2.5 1.5 1.0 0
	Sodium	≤2400 mg	Same as for < 50 y	2.5
		2401–3400 mg		1.5
		>3400 mg		0
	Alcohol (women):	≤1 drink/d	Same as for < 50 y	2.5
		1.01–1.5 drink/d		1.5
		1.51–2 drink/d		0
	Teaspoons of added sugar from muffins and biscuits, candy bars, pancakes and waffles, pie, sweetened soda, candies, chocolate, cookies, cakes, sweet rolls, coffee cake, pastries, jam honey, sherbet, ice cream	Added sugar:[3] ≤12 tsp/d 12.1–18 tsp/d 18.1–24 tsp/d ≥24 tsp/d	≤7.5 tsp/d 7.6–11.25 tsp/d 11.26–15 tsp/d >15 tsp/d	2.5 1.5 1.0 0
				Total score = sodium + alcohol + added fat + added sugar

[1] AI, adequate intake; RDA, recommended dietary allowance.

[2] Based on 2200 kcal for the <50 y category and 1900 kcal for the >51 y category.

Recommended Food Score (2, 4)[1]

Food group	Foods included
Vegetables	Tomatoes, broccoli, spinach, kale, carrots, iceberg lettuce, yams, potatoes, beans, string beans, corn, peas, mixed vegetables, celery, yellow squash, eggplant, romaine lettuce, tomato juice, tomato sauce, cabbage, cauliflower, Brussels sprouts, beets
Fruit	Apples or pears, oranges, cantaloupe, orange juice, grapefruit juice, grapefruit, other fruit juices, banana, apple juice, strawberries, blueberries, peaches, raisins, watermelon, applesauce, prunes
Protein	Chicken or turkey without skin, other fish, dark fish, canned tuna, tofu, shrimp
Grains	Dark breads, whole-grain cereals (predefined write-ins), cooked cereals, oatmeal, brown rice
Dairy	Skim milk
Maximum score	51

[1] 1 point for each item consumed at least weekly.

Alternate Mediterranean Diet Score (5, 6)

Food group	Foods included	Criteria for 1 point[1]
Vegetables	All vegetables except potatoes	Greater than median intake (servings/d)
Legumes	Tofu, string beans, peas, beans	Greater than median intake (servings/d)
Fruit	All fruit and juices	Greater than median intake (servings/d)
Nuts	Nuts, peanut butter	Greater than median intake (servings/d)
Whole grains	Whole-grain ready-to-eat cereals, cooked cereals, crackers, dark breads, brown rice, other grains, wheat germ, bran, popcorn	Greater than median intake (servings/d)
Red and processed meats	Hot dogs, deli meat, bacon, hamburger, beef	Less than median intake (servings/d)
Fish	Fish and shrimp, breaded fish	Greater than median intake (servings/d)
Ratio of monounsaturated to saturated fat	—	Greater than median intake (servings/d)
Ethanol	Wine, beer, "light" beer, liquor	5–25 g/d

[1] 0 points if these criteria are not met.

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