Major dietary patterns are related to plasma concentrations of markers of inflammation and endothelial dysfunction[1–3]

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ABSTRACT

Background: Endothelial dysfunction is one of the mechanisms linking diet and the risk of cardiovascular disease.

Objective: We evaluated the hypothesis that dietary patterns (summary measures of food consumption) are directly associated with markers of inflammation and endothelial dysfunction, particularly C-reactive protein (CRP), interleukin 6, E-selectin, soluble intercellular adhesion molecule 1 (sICAM-1), and soluble vascular cell adhesion molecule 1 (sVCAM-1).

Design: We conducted a cross-sectional study of 732 women from the Nurses' Health Study I cohort who were 43–69 y of age and free of cardiovascular disease, cancer, and diabetes mellitus at the time of blood drawing in 1990. Dietary intake was documented by using a validated food-frequency questionnaire in 1986 and 1990. Dietary patterns were generated by using factor analysis.

Results: A prudent pattern was characterized by higher intakes of fruit, vegetables, legumes, fish, poultry, and whole grains, and a Western pattern was characterized by higher intakes of red and processed meats, sweets, desserts, French fries, and refined grains. The prudent pattern was inversely associated with plasma concentrations of CRP ($P = 0.02$) and E-selectin ($P = 0.001$) after adjustment for age, body mass index (BMI), physical activity, smoking status, and alcohol consumption. The Western pattern showed a positive relation with CRP ($P < 0.001$), interleukin 6 ($P = 0.006$), E-selectin ($P < 0.001$), sICAM-1 ($P < 0.001$), and sVCAM-1 ($P = 0.008$) after adjustment for all confounders except BMI; with further adjustment for BMI, the coefficients remained significant for CRP ($P = 0.02$), E-selectin ($P < 0.001$), sICAM-1 ($P = 0.002$), and sVCAM-1 ($P = 0.02$).

Conclusion: Because endothelial dysfunction is an early step in the development of atherosclerosis, this study suggests a mechanism for the role of dietary patterns in the pathogenesis of cardiovascular disease. *Am J Clin Nutr* 2004;80:1029–35.

KEY WORDS Dietary patterns, inflammation, endothelial dysfunction, women, C-reactive protein

INTRODUCTION

Atherosclerosis is an inflammatory disease that begins with dysfunction of the vascular endothelium (1, 2). Endothelial dysfunction consists of enhanced and maintained endothelial activation reflected by elevated plasma concentrations of soluble endothelial adhesion molecules. The concentrations of these molecules are elevated in patients with all types of cardiovascular disease (CVD) and in patients who do not have clinically manifested CVD but who have coronary risk factors, such as smoking, hypertension, hypercholesterolemia, and diabetes mellitus (3). In addition, markers of systemic inflammation and endothelial dysfunction are predictors of CVD (4) and diabetes (5). Dietary interventions involving supplementation with single nutrients, such as n−3 fatty acids, folic acid, and antioxidants, may be effective in reducing systemic inflammation and reversing endothelial dysfunction (3).

The application of dietary patterns has recently become of considerable interest in nutritional epidemiology (6–8). Major dietary patterns, as summary variables of dietary intake, have been related to CVD risk in general populations (9–12). Furthermore, dietary patterns have shown a relation to some plasma markers of CVD risk and metabolic syndrome (13–15), such as plasma lipids, thrombogenic factors, and glycemic indicators. Except for C-reactive protein (CRP) (13), we are unaware of a relation between dietary patterns and plasma markers of inflammation and endothelial dysfunction. In this study, we evaluated whether dietary patterns derived from factor analysis were directly associated with markers of inflammation and endothelial dysfunction, including 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 cohort was established in 1976 with 121 700 female registered nurses residing in the United States.

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Every 2 y, follow-up questionnaires have been sent to update information on potential risk factors and to identify newly diagnosed cases of chronic diseases. The present study included 732 women who were selected as control subjects for a nested case-control study on diabetes that is currently underway. These women did not have CVD, cancer, or diabetes mellitus at the time of blood drawing. The average age of the women at the time of blood drawing was 56 y (range: 43–69 y). All participants gave written informed consent, and the Harvard School of Public Health Human Subjects Committee Review Board approved the study protocol.

Blood collection and assessment of biomarkers

Blood was collected between 1989 and 1990. Women who were willing to provide blood specimens were sent instructions and a phlebotomy kit. Blood specimens were returned by overnight mail on ice, and 97% arrived within 26 h of phlebotomy. The samples were centrifuged ($1200 \times g$, 15 min, room temperature) on arrival to separate plasma from buffy coat and red blood cells and were frozen in liquid nitrogen until analysis. Quality-control samples were routinely frozen along with study samples to monitor plasma changes due to long-term storage and to monitor changes in assay variability. Study samples were analyzed in randomly ordered case-control pairs to further reduce systematic bias and interassay variation.

All markers were measured in the Clinical Chemistry Laboratory at Children's Hospital in Boston. CRP concentrations were measured by using a latex-enhanced turbidimetric assay on a Hitachi 911 (Denka Seiken, Tokyo). IL-6 concentrations were measured by using an ultrasensitive enzyme-linked immunosorbent assay from R & D Systems (Minneapolis). Concentrations of E-selectin, sICAM-1, and sVCAM-1 were measured by using a commercial enzyme-linked immunosorbent assay (R&D Systems). The interassay CVs for the biomarkers were as follows: CRP, 3.4–3.8%; IL-6, 5.8–8.2%; E-selectin, 6.4–6.6%; sICAM-1, 6.1–10.1%; sVCAM-1, 8.5–10.2%.

Assessment of dietary intake

In 1986 and 1990, a semiquantitative food-frequency questionnaire (FFQ) was mailed to participants. The FFQ included questions on 116 food items with specified serving sizes that were described by using natural portions or standard weight and volume measures of servings commonly consumed in this study population. For each food item, participants indicated their average frequency of consumption over the past year in terms of the specified serving size by checking 1 of 9 frequency categories, which ranged from "almost never" to "≥ 6 times/d." The selected frequency category for each food item was converted to a value in number of servings per day. The reproducibility and validity of the FFQ used in this study has been reported elsewhere (16). We aggregated single food items into 37 predefined food groups to minimize within-person variation in consumption of individual foods. Individual food items were preserved if they constituted distinct items on their own (eg, eggs, butter, margarine, pizza, soup, coffee, and tea) or if they were thought to represent particular dietary habits (eg, liquor, wine, beer, and French fries) (**Appendix A**). We calculated the averages of food or food groups in 1986 and 1990 to represent long-term dietary patterns and to reduce measurement error in the case of women who provided such information in both years (n = 651); for those who did not, we used the food consumption data reported on either the 1986 or the 1990 FFQ.

Assessment of other variables

Cigarette smoking and body weight were assessed in 1990. Body mass index (BMI) was calculated as weight (in kg)/height^2 (in m). Physical activity was assessed in hours per week spent on common leisure-time physical activities expressed as metabolic equivalent hours per week (MET-h/wk) (17).

Statistical analysis

The procedure for deriving dietary patterns by using food-consumption data from the FFQ has been described in detail elsewhere (18). We conducted principal component analysis to derive dietary patterns based on food groups (19). The factors were rotated by an orthogonal transformation, which maintains uncorrelated factors and achieves a simpler structure with greater interpretability. To determine the number of factors to be retained, we considered the criterion of an eigenvalue >1, the Scree test (20), and the interpretability of the factors. We did not use the percentage of variance explained by each factor because this criterion depends largely on the total number of variables included in the analyses (20). The factor score for each pattern was constructed by summing observed intakes of the component food items weighted by factor loadings, so each woman received a factor score for each identified pattern (20). The analyses were conducted with the use of the PROC FACTOR procedure in SAS (21). We derived the dietary patterns by using the FFQ administered in 1986, the FFQ administered in 1990, and the average of the 2 FFQs, respectively.

We used PROC GLM to calculate means and CIs for the markers in each quintile of the patterns. We used the log-transformed markers as the dependent variable and the score for each pattern categorized in quintiles as the independent variable. Then we calculated the exponential values of the means and the CIs to obtain the means for the markers.

Multiple linear regressions were used to assess the relation between plasma concentrations of endothelial markers and dietary patterns. We used log-transformed plasma concentrations of biomarkers to achieve normal distributions. First, we adjusted for age (≤45, 46–50, 51–55, 56–60, 61–65, ≥66 y), physical activity (<1.5, 1.5–5.9, 6.0–11.9, 12.0–20.9, ≥21.0 metabolic equivalent h/wk), smoking status (never; past; current, 1–14 cigarettes/d; current, ≥15 cigarettes/d), and alcohol consumption (nondrinker, 0–4.9, 5.0–10.0, >10.0 g/d) but not for BMI because it might be an intermediate factor in the causal pathway between dietary patterns and CVD. In an additional analysis, we also adjusted for BMI (<23.0, 23.0–24.9, 25.0–29.9, 30.0–34.9, ≥35.0).

RESULTS

The 2 major dietary patterns identified by factor analysis were qualitatively similar across time (1986–1990) (**Table 1**). The prudent pattern was characterized by higher intakes of vegetables, fruit, legumes, whole grains, fish, and poultry, whereas the Western pattern was characterized by higher intakes of red meat, processed meat, refined grains, sweets, desserts, French fries, and high-fat dairy products.

TABLE 1
Factor-loading matrix for dietary patterns from food-frequency questionnaires completed by women[1]

	Prudent			Western		
Foods	1986	1990	1986, 1990[2]	1986	1990	1986, 1990[2]
Other vegetables	0.73	0.68	0.73	—	—	—
Green, leafy vegetables	0.66	0.65	0.68	—	—	—
Dark-yellow vegetables	0.62	0.65	0.66	—	—	—
Cruciferous vegetables	0.59	0.61	0.62	—	—	—
Fruit	0.58	0.58	0.60	—	—	—
Tomatoes	0.56	0.49	0.55	0.16	0.16	0.18
Fish and other seafood	0.53	0.51	0.55	—	—	—
Legumes	0.51	0.57	0.55	0.20	—	0.18
Poultry	0.42	0.42	0.44	—	—	—
Salad dressings	0.40	0.34	0.39	—	—	—
Fruit juices	0.24	0.21	0.25	—	—	0.15
Water	NA	0.32	NA	NA	—	NA
Processed meats	—	—	—	0.57	0.58	0.59
Refined grains	—	—	—	0.57	0.52	0.58
Red meats	—	—	—	0.56	0.60	0.61
Sweets and desserts	—	—	—	0.49	0.45	0.49
French fries	—	—	—	0.48	0.46	0.49
High-fat dairy products	—	—	—	0.40	0.46	0.45
Potatoes	—	0.21	0.16	0.38	0.33	0.39
Pizza	—	—	—	0.34	0.36	0.37
Sugar-containing beverages	—	—	—	0.34	0.33	0.36
Mayonnaise and other creamy salad dressings	0.20	—	0.16	0.33	0.34	0.36
Condiments	0.17	—	—	0.33	0.37	0.38
Eggs	—	—	—	0.32	0.41	0.38
Snacks	—	—	—	0.31	0.29	0.31
Margarine	—	—	—	0.30	0.32	0.34
Cream soup	0.15	—	—	0.30	0.31	0.32
Other soups	0.27	NA	NA	0.28	NA	NA
Butter	—	—	—	0.25	0.29	0.29
Nuts	0.21	0.17	0.20	0.22	0.23	0.24
Tea	—	—	—	0.17	—	0.16
Organ meats	—	—	—	—	—	—
Liquor	—	—	—	—	—	—
Olive oil	NA	0.31	NA	NA	—	NA
Wine	—	—	—	—	—	—
Coffee	—	—	—	—	—	—
Sugar-free beverages	—	—	—	—	—	—
Beer	—	—	—	—	—	—
Whole grains	0.38	0.41	0.41	—	—	—
Low-fat dairy products	0.30	0.32	0.32	—	—	—

[1] *See* Appendix A for food groupings. NA, data not available; —, $< \pm 0.15$.
[2] Average consumption from food-frequency questionnaires administered in 1986 and 1990.

In comparison with the subjects in the lowest quintile of the prudent pattern, those in the higher quintiles were more physically active and smoked less (P for trend of means across quintiles = 0.002 and 0.001, respectively) (**Table 2**). In addition, the subjects in the higher quintiles of the prudent pattern had lower intakes of saturated fat and *trans* fatty acids but higher intakes of polyunsaturated fat, folate, and fiber (P for trend was significant for all). In contrast, in comparison with the subjects in the lowest quintile of the Western pattern, those in the higher quintiles had higher BMI (P for trend < 0.001), were more likely to smoke ($P = 0.006$), and were less likely to exercise ($P = 0.04$). Furthermore, the subjects in the higher quintiles of the Western pattern had higher intakes of saturated fat and *trans* fatty acids but lower intakes of folate and fiber (P for trend was significant for all).

Almost all markers were correlated, but the correlations were only modest (**Table 3**). Age-adjusted geometric mean plasma concentrations of CRP and E-selectin showed significant decreasing trends with increasing quintiles of the prudent pattern (P for trend of medians: 0.05 for CRP and < 0.001 for E-selectin) (**Table 4**). In contrast, CRP, E-selectin, sICAM-1, and sVCAM-1 showed increasing trends with increasing quintiles of the Western pattern (P for trend of medians: 0.04 for CRP, 0.02 for E-selectin, 0.008 for sICAM-1, and 0.04 for sVCAM).

β coefficients between the patterns generated from food-consumption data, averaged over 1986 and 1990, and the log-transformed biomarkers are shown in **Table 5**. We chose the average food-consumption values because they reflect maintained habits during the time. The prudent pattern was inversely

TABLE 2
Baseline characteristics according to quintiles of dietary pattern scores in the Nurses' Health Study[1]

	Quintile of prudent pattern score				Quintile of Western pattern score			
Subject characteristic	1 (lowest)	3	5 (highest)	*P* for trend	1 (lowest)	3	5 (highest)	*P* for trend
Age (y)	54.0 ± 7.1[2]	55.9 ± 6.3	57.8 ± 6.6	<0.001	58.1 ± 6.3	56.4 ± 6.8	54.7 ± 7.0	<0.001
BMI (kg/m^2)	26.2 ± 6.6	27.1 ± 6.6	26.8 ± 6.3	0.03	25.1 ± 4.7	26.0 ± 5.9	28.1 ± 7.5	<0.001
Physical activity (MET-h/wk)	11.1 ± 18.3	12.6 ± 14.8	15.4 ± 17.8	0.002	14.3 ± 14.2	12.7 ± 11.9	11.4 ± 18.0	0.04
Alcohol consumption (g/d)	4.6 ± 7.3	6.7 ± 8.4	6.5 ± 10.0	0.05	5.7 ± 9.5	6.7 ± 10.3	6.3 ± 9.7	0.18
Current smoker (%)	26.7	11.8	8.3	<0.001	9.2	18.0	14.8	0.006
Energy intake (kcal/d)	1476.7 ± 432.2	1777.1 ± 446.5	2081.2 ± 431.2	<0.001	1348.6 ± 337.1	1755.1 ± 336.7	2274.8 ± 371.3	<0.001
Nutrient intakes[3]								
Cholesterol (mg/d)	236.6 ± 76.6	241.0 ± 56.7	225.2 ± 62.2	0.02	215.0 ± 67.7	230.0 ± 59.5	247.3 ± 61.0	<0.001
Saturated fat (g/d)	21.7 ± 4.3	20.4 ± 3.5	18.0 ± 3.9	<0.001	17.3 ± 4.3	20.0 ± 3.9	21.9 ± 3.6	<0.001
Monounsaturated fat (g/d)	23.0 ± 4.1	22.1 ± 3.4	19.7 ± 3.8	<0.001	18.9 ± 4.0	21.2 ± 3.4	23.7 ± 3.0	<0.001
Polyunsaturated fat (g/d)	10.1 ± 2.3	11.0 ± 2.3	11.3 ± 2.8	<0.001	10.4 ± 2.8	10.4 ± 2.2	11.3 ± 2.4	<0.001
trans Fat (g/d)	3.1 ± 1.0	2.6 ± 0.7	2.1 ± 0.7	<0.001	2.0 ± 0.7	2.5 ± 0.7	3.0 ± 0.7	<0.001
Folate (μg/d)	344.6 ± 189.9	436.0 ± 184.7	489.4 ± 181.7	<0.001	478.8 ± 233.9	441.9 ± 179.7	359.7 ± 147.4	<0.001
Fiber (g/d)	13.8 ± 3.2	17.8 ± 3.4	22.6 ± 6.9	<0.001	21.0 ± 7.1	17.6 ± 5.0	15.9 ± 3.4	<0.001
Protein (g/d)	69.2 ± 11.3	75.0 ± 9.9	80.6 ± 12.0	<0.001	79.5 ± 13.8	74.4 ± 11.2	72.5 ± 9.0	<0.001
Carbohydrate (g/d)	194.1 ± 26.5	190.8 ± 25.3	200.4 ± 32.3	<0.001	206.2 ± 34.6	196.7 ± 30.5	185.6 ± 24.3	<0.001
Glycemic load	10 460 ± 1710	9906 ± 1605	10 056 ± 1882	0.004	10 483 ± 2173	11 224 ± 2012	9874 ± 1532	0.11

[1] MET-h/wk, metabolic equivalent (energy need per kilogram of body weight per hour of activity divided by the energy need per kilogram of body weight per hour at rest) hours per week.
[2] $\bar{x}$ ± SD (all such values).
[3] Energy adjusted.

related to plasma concentrations of CRP ($P = 0.02$) and E-selectin ($P = 0.001$) after adjustment for age, BMI, physical activity, smoking status, and average alcohol consumption. We did not see important differences between the β coefficients before and after adjustment for BMI. The Western pattern showed a positive relation with CRP ($P < 0.001$), IL-6 ($P = 0.006$), E-selectin ($P < 0.001$), sICAM-1 ($P < 0.001$), and sVCAM-1 ($P = 0.008$) after adjustment for all confounders except BMI; with adjustment for BMI, the β coefficients for CRP ($P = 0.02$), E-selectin ($P < 0.001$), sICAM (0.002), and sVCAM-1 ($P = 0.02$) remained significant. Additional adjustment for energy intake, fasting status, aspirin use, and use of hormone replacement therapy did not modify the associations.

In a secondary analysis, we examined the associations between individual foods and food groups in each pattern and the markers of inflammation and endothelial dysfunction. As expected, the foods belonging to the prudent pattern generally showed an inverse association with the biomarkers, whereas the foods belonging to the Western pattern showed a positive association (data not shown). However, most of these associations were weaker than those for the 2 major dietary patterns.

DISCUSSION

In this study of apparently healthy women, we found an inverse relation between a prudent dietary pattern and plasma concentrations of CRP and E-selectin and a positive relation between a Western dietary pattern and concentrations of CRP, IL-6, E-selectin, sICAM-1, and sVCAM-1. The association between the Western dietary pattern and IL-6 can partly be explained by BMI.

CRP and IL-6 are markers of systemic inflammation and independent predictors of CVD in healthy women (4). Recent data suggest that CRP plays an active role in atherogenesis (22). E-selectin, sICAM-1, and sVCAM-1 are markers of endothelial dysfunction that are detectable in the circulation. Higher concentrations of E-selectin and sICAM-1 have been observed in patients with ischemic heart disease (23), and baseline plasma concentrations of sICAM-1 are predictors of myocardial infarction in apparently healthy men (24). sVCAM-1 is mainly expressed in atherosclerotic plaques and is considered a marker of advanced atherosclerosis (25). Therefore, our findings relating dietary patterns to CRP, E-selectin, sICAM-1, and sVCAM-1 might reflect a potential pathway to CVD.

TABLE 3
Pearson correlation coefficients for log-transformed markers[1]

	Log CRP	Log IL-6	Log E-selectin	Log sICAM-1	Log sVCAM-1
Log CRP	1	0.33 (<0.001)	0.23 (<0.001)	0.16 (<0.001)	0.06 (0.09)
Log IL-6		1	0.24 (<0.001)	0.18 (<0.001)	0.11 (0.003)
Log E-selectin			1	0.39 (<0.001)	0.27 (<0.001)
Log sICAM-1				1	0.40 (<0.001)
Log sVCAM-1					1

[1] P values in parentheses. CRP, C-reactive protein; IL-6, interleukin 6; sICAM-1, soluble intercellular adhesion molecule 1; sVCAM-1, soluble vascular cell adhesion molecule 1.

TABLE 4
Plasma concentrations of biomarkers by quintile (Q) of dietary pattern scores[1]

Dietary pattern[2]	CRP	IL-6	E-selectin	sICAM-1	sVCAM-1
	mg/dL	*pg/mL*	*pg/mL*	*ng/mL*	*ng/mL*
Prudent					
Q1	0.15 (0.12, 0.18)	1.9 (1.7, 2.2)	48.2 (44.7, 52.0)	247 (237, 258)	537 (513, 562)
Q2	0.17 (0.15, 0.21)	1.9 (1.7, 2.1)	45.1 (42.1, 48.3)	252 (243, 262)	545 (523, 568)
Q3	0.16 (0.13, 0.19)	1.8 (1.7, 2.1)	44.6 (41.5, 47.8)	251 (241, 261)	521 (499, 543)
Q4	0.14 (0.12, 0.16)	1.8 (1.6, 2.0)	43.7 (40.9, 46.6)	248 (240, 257)	532 (512, 553)
Q5	0.13 (0.11, 0.16)	1.8 (1.6, 2.0)	40.1 (37.5, 43.0)	242 (233, 251)	505 (484, 526)
P for trend	0.05	0.32	<0.001	0.26	0.03
Western					
Q1	0.12 (0.10, 0.15)	1.8 (1.6, 2.0)	41.8 (38.8, 45.0)	246 (236, 256)	507 (486, 530)
Q2	0.15 (0.13, 0.18)	1.8 (1.6, 2.0)	44.0 (41.1, 47.0)	238 (230, 247)	514 (493, 535)
Q3	0.15 (0.12, 0.17)	1.9 (1.7, 2.1)	44.1 (41.3, 47.2)	248 (239, 258)	539 (518, 561)
Q4	0.16 (0.13, 0.19)	1.8 (1.6, 2.0)	43.3 (40.5, 46.3)	247 (238, 256)	543 (522, 565)
Q5	0.17 (0.14, 0.20)	2.0 (1.8, 2.3)	47.9 (44.5, 51.5)	262 (252, 273)	535 (512, 559)
P for trend	0.04	0.16	0.02	0.008	0.04

[1] All values are geometric $\bar{x}$; 95% CI in parentheses. CRP, C-reactive protein; IL-6, interleukin 6; sICAM-1, soluble intercellular adhesion molecule 1; sVCAM-1, soluble vascular cell adhesion molecule 1; MET-h/wk, metabolic equivalent (energy need per kilogram of body weight per hour of activity divided by the energy need per kilogram of body weight per hour at rest) hours per week. Values were adjusted for age (≤45, 46–50, 51–55, 56–60, 61–65, ≥66 y), BMI (in kg/m^2) in 1990 (<23.0, 23.0–24.9, 25.0–29.9, 30.0–34.9, ≥35. 0), physical activity in 1990 (<1.5, 1.5–5.9, 6.0–11.9, 12.0–20.9, ≥21.0 MET-h/wk), smoking status (never; past; current, 1–14 cigarettes/d; current, ≥15 cigarettes/d), and average alcohol consumption between 1986 and 1990 (nondrinker; 0–4.9, 5.0–10.0, >10.0 g/d).

[2] Average consumption between 1986 and 1990. Quintiles were calculated by summing intakes of food groups weighted by their factor loadings.

Diets that are high in fruit, vegetables, antioxidant vitamins, folic acid, and n−3 fatty acids appear to have at least 2 beneficial effects on vascular endothelial function: *1*) they decrease endothelial activation, and *2*) they improve endothelium-dependent vasodilation (3). In contrast, diets that are high in *trans* fatty acids may impair endothelial function (26). Our study is consistent with the above evidence because the prudent pattern reflects a high consumption of fruit (source of antioxidant vitamins), vegetables (source of folic acid), and fish (source of n−3 fatty acids), whereas the Western pattern reflects a high consumption of margarine, commercially baked products, and deep-fried fast food (sources of *trans* fatty acids). Moreover, a prudent dietary pattern was associated with lower CRP concentrations in a study of male health professionals (13).

Insulin resistance syndrome and obesity are closely linked to atherosclerosis and may enhance the inflammatory process present in all stages of atherosclerosis (27). Hyperglycemia associated with insulin resistance can lead to modification of macromolecules as advanced glycation end products that bind surface receptors, which augment the production of proinflammatory cytokines in vascular endothelial cells. Elevated concentrations of CRP and IL-6 have been shown to predict the development of type 2 diabetes mellitus (5). In addition, adipose tissue secretes cytokines, which stimulate the production of acute phase proteins such as CRP. Several cross-sectional studies found a relation between obesity and markers of inflammation and endothelial activation (28–30). In our analysis, dietary patterns were associated with plasma biomarkers of inflammation and endothelial dysfunction after exclusion of subjects with diabetes mellitus and after control for BMI, which suggests that the effect of diet on the development of atherosclerosis is not fully mediated through the development of diabetes and obesity.

The β coefficients for the relation between the patterns and the markers were low because we used log-transformed concentrations of the markers. We found differences as large as 32 units between quintiles 1 and 5 of the prudent pattern for sVCAM-1.

TABLE 5
β regression coefficients for the relation between prudent and Western dietary pattern scores and log-transformed biomarkers[1]

	Prudent			Western		
	Model 1	Model 2	Model 3	Model 1	Model 2	Model 3
Log CRP	−0.07 (0.10)	−0.07 (0.13)	−0.10 (0.02)	0.20 (<0.001)	0.21 (<0.001)	0.10 (0.02)
Log IL-6	−0.03 (0.30)	−0.02 (0.39)	−0.03 (0.21)	0.08 (0.003)	0.08 (0.006)	0.04 (0.12)
Log E-selectin	−0.06 (<0.001)	−0.05 (0.005)	−0.05 (0.001)	0.08 (<0.001)	0.08 (<0.001)	0.06 (<0.001)
Log sICAM-1	−0.01 (0.17)	−0.004 (0.65)	−0.01 (0.54)	0.04 (<0.001)	0.04 (<0.001)	0.03 (0.002)
Log sVCAM-1	−0.002 (0.85)	−0.01 (0.55)	−0.01 (0.48)	0.02 (0.06)	0.03 (0.008)	0.02 (0.02)

[1] *P* values in parentheses. CRP, C-reactive protein; IL-6, interleukin 6; sICAM-1, soluble intercellular adhesion molecule 1; sVCAM-1, soluble vascular cell adhesion molecule 1; MET-h/wk, metabolic equivalent (energy need per kilogram of body weight per hour of activity divided by the energy need per kilogram of body weight per hour at rest) hours per week. Model 1 was unadjusted. Model 2 was adjusted for age (≤45, 46–50, 51–55, 56–60, 61–65, ≥66 y), physical activity in 1990 (<1.5, 1.5–5.9, 6.0–11.9, 12.0–20.9, ≥21.0 MET-h/wk), smoking status (never; past; current, 1–14 cigarettes/d; current, ≥15 cigarettes/d), and average alcohol consumption between 1986 and 1990 (nondrinker; 0–4.9, 5.0–10.0, >10.0 g/d). Model 3 was adjusted for all factors in model 2 plus BMI (in kg/m^2) in 1990 (<23.0, 23.0–24.9, 25.0–29.9, 30.0–34.9, ≥35.0).

However, the cumulative effects on multiple biomarkers are likely to be much greater than the effect on a single marker.

This study had some limitations. First, it was cross-sectional, so we cannot infer causality from our results, although we can assume a certain directionality because some dietary information was collected 4 y before the blood draw. Second, there was some degree of error in the measurement of food consumption. However, the use of the repeated measurement enabled us to reduce within-person random error. Third, the factor analysis approach involved several arbitrary but important decisions, including the consolidation of food items into food groups, the number of factors to be extracted, the method of rotation, and the labeling of the components (6). However, our 2 main patterns have been used in previous studies in men and women, and these patterns have been shown to predict the risks of CVD and other chronic diseases (9, 11, 13, 31). Finally, dietary patterns may differ by sex, race, cultural group, and geographical region; thus, our study population of US women, most of whom were white and had a comparatively high educational level, may not be generalizable to other populations. However, similar patterns have been identified in nationally representative samples (32).

In conclusion, the present study supports the hypothesis that major dietary patterns are associated with markers of inflammation and endothelial dysfunction. Our findings suggest that one mechanism underlying the relation between diet and CVD may involve influencing the process of systemic inflammation and endothelial dysfunction.

The study was conceived and designed by EL-G, MBS, TTF, JEM, and FBH. JBM, NR, JEM, and FBH were responsible for acquisition of data. EL-G, MBS, TTF, JBM, NR, JEM, and FBH analyzed and interpreted the data. EL-G wrote the draft of the manuscript. The manuscript was critically revised for important intellectual content by EL-G, MBS, TTF, JBM, NR, JEM, and FBH. EL-G, MBS, TTF, and FBH provided statistical expertise. JEM and FBH obtained funding and provided administrative, technical, and material support. The study was supervised by FBH. None of the authors had any conflicts of interest.

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APPENDIX A

Food groupings used in the dietary pattern analyses

Foods or food groups	Food items
Processed meats	Processed meats, bacon, hot dogs
Red meats	Beef, pork, lamb, hamburger
Organ meats	Beef, calf, and pork liver; chicken and turkey liver
Fish and other seafood	Canned tuna fish, dark-meat fish, other fish, shrimp, lobster, scallops
Poultry	Chicken or turkey with or without skin
Eggs	Eggs
Butter	Butter
Margarine	Margarine
Olive oil	Olive oil
Low-fat dairy products	Skim or low-fat milk, sherbet or ice milk, yogurt
High-fat dairy products	Whole milk, cream, sour cream, ice cream, cream cheese, other cheese
Liquor	Liquor
Wine	Red wine, white wine
Beer	Beer
Tea	Tea
Coffee	Coffee
Fruit	Raisins or grapes, avocado, bananas, cantaloupe, watermelon, fresh apples or pears, oranges, grapefruit, strawberries, blueberries, peaches, apricots, plums
Fruit juices	Apple juice or cider, orange juice, grapefruit juice, other fruit juice
Cruciferous vegetables	Broccoli; coleslaw and uncooked cabbage; cauliflower; Brussels sprouts; kale, mustard, and chard greens; sauerkraut
Dark-yellow vegetables	Carrots, yellow (winter) squash, yams
Tomatoes	Tomatoes, tomato juice, tomato sauce
Green, leafy vegetables	Spinach, iceberg or head lettuce, romaine or leaf lettuce
Legumes	String beans, peas or lima beans, beans or lentils, tofu or soybeans, alfalfa sprouts
Other vegetables	Celery, mushrooms, green pepper, corn, mixed vegetables, eggplant, summer squash
Potatoes	Potatoes
French fries	French fries
Whole grains	Cooked oatmeal, other cooked breakfast cereal, dark bread, brown rice, other grains, bran added to food, wheat germ
Refined grains	White bread, English muffins, bagels or rolls, muffins or biscuits, white rice, pasta, pancakes or waffles
Pizza	Pizza
Snacks	Potato chips or corn chips, crackers, popcorn
Nuts	Peanuts, other nuts, peanut butter
Sugar-containing beverages	Cola with sugar, other carbonated beverages with sugar, fruit drinks
Sugar-free beverages	Low-energy cola, other low-energy carbonated beverages
Salad dressing	Oil-and-vinegar salad dressing
Mayonnaise and other creamy salad dressings	Mayonnaise and other creamy salad dressings
Cream soup	Chowder or cream soup
Other soups	Homemade soup, ready-made soup
Sweets and desserts	Chocolate bars or pieces, candy bars, cookies, brownies, doughnuts, cake, pie, sweet roll, coffee cake, pastry
Condiments	Red chili sauce (dry or prepared), mustard, pepper, soy or Worcestershire sauce, jam, jelly, syrup, honey