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Diet quality and markers of endothelial function: the CARDIA study

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Abstract

Background: Dietary patterns are associated cross-sectionally with cellular adhesion molecules (CAMs).

Objective: We studied prospective associations of three dietary patterns with CAMs.

Design: In the Coronary Artery Risk Development in Young Adults (CARDIA) study, diet was assessed at years 0 (1985-86) and 7 (1992-93) examinations. Four circulating CAMs (E-selectin, P-selectin, soluble intercellular adhesion molecule 1 (sICAM-1), and vascular cellular adhesion molecule (VCAM)) were assayed at years 7 and 15 (2000-01). We created one index score "*A Priori* Diet Quality Score" and derived dietary patterns using principal components analysis (PCA). Multivariable linear regression models predicted year 15 CAMs from averaged (year 0/7) dietary patterns.

Results: The *A Priori* Diet Quality Score rated 46 food groups beneficial, neutral or adverse based on hypothesized health effects. We derived two PCA dietary patterns: "fruit and vegetables (FV)" (high intakes of fruit, vegetables, and whole grains) and "meat" (high intakes of red meat, refined grain, and butter). All dietary patterns were related to E-selectin and sICAM-1. P-selectin was not related to the FV dietary pattern. VCAM was only related to the *A Priori* Diet Quality Score. Strongest associations were for the meat dietary pattern with E-selectin (effect size 28% of an SD (+3.9/13.7 ng/mL) and P-selectin (effect size 37% of an SD (+4.1/11.2 ng/mL) and the *A*

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Priori Diet Quality Score with sICAM-1 (effect size 34% of an SD (−15.1/44.7 ng/mL) and VCAM (effect size of 26% of an SD (−45.1/170.3 ng/mL).

Conclusion: This prospective analysis suggests that dietary patterns are associated with CAMs.

Keywords

Cohort; Epidemiology; Diet; Endothelial function; Cellular Adhesion Molecules (CAMs)

Introduction

Endothelial dysfunction occurs early in atherosclerotic development (1). The cellular adhesion molecules (CAMs) E-selectin, P-selectin, intercellular adhesion molecule-1 (ICAM-1), and vascular cellular adhesion molecule (VCAM), are expressed by inflamed endothelium and participate in recruitment and adhesion of leucocytes to endothelial cells (2). Higher circulating concentrations of these CAMs indicate endothelial dysfunction, promote atherosclerosis, and associate with subclinical cardiovascular disease (3). Diet influencing endothelial function may be a mechanism by which dietary quality affects the development of cardiovascular disease.

Clinical and experimental studies suggested that dietary n-3 fatty acids, antioxidant vitamins, folic acid, and L-arginine have beneficial effects on endothelial function, likely through multiple, complex mechanisms. Examples are inhibition of monocyte adhesion and platelet activation, increased nitric-oxide production and improvement of vasodilation, and blockage of lipid oxidation (4). Randomized cross-over trials showed that Mediterranean-style diets improved endothelial function (5, 6). Cross-sectional studies found inverse associations between principal components analysis (PCA)-derived dietary patterns and markers of endothelial function in women (7) and in ethnically diverse men and women (8). Some, but not all, cross-sectional associations of different prudent dietary patterns were inverse with endothelial function (9). One longitudinal study investigated consumption of food groups and markers of endothelial function, but overall dietary pattern was not assessed (10). Associations of dietary patterns with markers of endothelial function have not been investigated in prospective studies.

We hypothesized that the *A Priori* Diet Quality Score and the FV dietary pattern with high loadings on fruit and vegetables is inversely related to E-selectin, P-selectin, sICAM-1, and VCAM. Similarly, we hypothesize that the meat dietary pattern with high loadings of meat, butter, and refined grains is positively related to these CAMs.

Methods

Study sample

The Coronary Artery Risk Development in Young Adults (CARDIA) Study is a multicenter, longitudinal investigation of the evolution of coronary heart disease risk starting in young adulthood (11). CARDIA recruited a population-based sample of 5115 black and white men and women aged 18-30 years in Birmingham, AL; Chicago, IL; Minneapolis, MN; and Oakland, CA. Recruitment achieved roughly equal proportions of blacks (51.5%) and whites

(48.5%), men (45.5%) and women (54.5%), ages 18-24 y (44.9%) and 25-30 y (55.1%), and with ≤high school education (39.7%) or >high school education (60.3%). For the present study, we used dietary data collected at baseline (1985-86) and after 7 years of follow-up (1992-93). The response rates were 81% at year 7 and 74% at year 15 (2000-01). Young Adult Longitudinal Trends in Antioxidants (YALTA) and Circulating CAMs and the Vasculature are CARDIA ancillary studies in which the CAMs E-selectin, P-selectin, sICAM-1, and VCAM were measured in year 7 and year 15. Institutional Review Board approval and informed consent were obtained at each study center at every examination. Participants who had missing dietary data (n=4 at year 0 and n=143 at year 7), or implausibly high or low energy intake (<800 or >8000 kcal/day for men, <600 or >6000 kcal/day for women) (n=128 at year 0 and n=94 at years 7) were excluded from analysis. Accounting for analysis-specific exclusions due to missing data for relevant exposures or covariates, we included 2789 participants for the prospective analysis of year 15 values of E-selectin and the average of year 0 and 7 dietary patterns, 2947 for P-selectin, 2911 for sICAM-1, and 2998 for VCAM.

Blood collection and measurements of biomarkers

Overnight fasting blood samples were processed within 90 min of blood collection and stored at −70°C until shipped on dry ice to a central laboratory. Participants were asked to fast ≥12 hours and to avoid heavy physical activity and smoking for 2 hours before examination. CAMs were assayed at the Molecular Epidemiology and Biomarker Research Laboratory in the University of Minnesota with sandwich ELISA methods from R & D Systems (E-selectin Cat No: DSLE00, P-selectin Cat No: BBE6, sICAM-1 Cat. No. DCD540 (year 7) and DY720 (year 15), and VCAM Cat No. DVC00). Serum (E-selectin) and plasma (P-selectin) samples from year 7 and 15 exams were diluted 10- and 6-fold, respectively. The within plus between day coefficients of variation (CV) were 7.7 and 10.5%, respectively. The E-selectin measurements for years 7 and 15 were performed over a period of several months, and no assay drift was evident during this time.

Serum (sICAM-1) samples from year 7 and 15 exams were diluted 10- and 400-fold and plasma (VCAM) samples 21-fold. The within plus between day CVs were < 10% (both sICAM-1 assays) and 9.0% (VCAM). All VCAM analyses of the year 7 and 15 samples were performed over a few months in 2010, and no assay drift was detected during this time. To account for assay drift (P-selectin), assay change and the prevalence of the single nucleotide polymorphism rs5491 T-allele (sICAM-1), P-selectin and sICAM-1 were calibrated (details in the online supplemental material).

Other measurements

Standard questionnaires were used to obtain self-reported demographic and behavioral information across CARDIA examinations. Information on sex, race, date of birth, education, and cigarette smoking was collected by structured interview or self-administered questionnaire at each examination. Educational status was quantified as the maximum (at any examination) reported number of years of schooling completed. Self-reported smoking status was classified as never, former, or current . A physical activity score was derived from the CARDIA Physical Activity History. The total exercise score was in exercise units

(a sum across 13 activities of frequency times intensity). Height and weight were measured at each examination and recorded to the nearest 0.5 cm and 0.2 kg, respectively. Body mass index (BMI) was calculated as weight(kg)/height^2 (m).

Dietary assessment and creation of dietary pattern scores

Diet assessment and the procedure for the creation of dietary patterns were described in detail elsewhere (12, 13). In summary diet was assessed at years 0 and 7 by interviewer-administered CARDIA Diet History (14).

Foods were assigned to one of 166 food groups using the food grouping system devised by the University of Minnesota Nutrition Coordinating Center (NCC). We further collapsed these food groups into 46 food groups based on similar nutrient characteristics and comparability to food groups defined in previous studies (15-17).

The *A Priori* Diet Quality Score was created by classifying 46 foods groups as beneficial (n=20), adverse (n=13), or neutral (n=13) in terms of hypothesized health effects(15-17). The *a priori* assignment for each of the 46 food groups (beneficial="+", adverse="-", neutral = "0") was described in detail elsewhere (12, 13) and can be found in Supplemental Table 2. The *A Priori* Diet Quality Score was the sum of category scores 0 to 4 for the beneficial items plus scores in reverse order (4 to 0) for adverse foods. Food groups that were considered neutral did not contribute to the overall *A Priori* Diet Quality Score. The theoretical maximum score was 132, higher scores indicating a healthier dietary pattern.

We used PCA with orthogonal rotation to derive uncorrelated dietary patterns and determine factor loadings for each of the 46 food groups. We selected the 2 principal components that explained the most dietary variance (Supplemental Table 2). We refer to these 2 factors as "meat dietary pattern" and "fruit and vegetable (FV) dietary pattern" to reflect their relatively high loadings of red meat (as well as refined grain and butter) or fruits and vegetables (as well as whole grains and lean fish), respectively. Factor loadings were generally consistent across years; factor loadings <0.20 were suppressed in Supplemental Table 2.

Statistics

Unadjusted means of participant characteristics were calculated by quintiles of *A Priori* Diet Quality Score and the two dietary patterns. Multivariable adjusted linear regression models assessed associations of dietary patterns (averaged year 0 and 7, using 1 exam if the other was missing), each divided into consumption quintiles, to predict E-selectin, P-selectin, sICAM-1, and VCAM prospectively for CAMs at year 15. Parallel cross-sectional analyses for CAMs at year 7 were examined in sensitivity analyses, as was ability to predict change in CAMs between year 7 and year 15.

Separate regression analyses were conducted for each dietary pattern. Tests for trend used multivariable linear regression models with continuous dietary pattern scores. We studied different levels of adjustment. A minimal model (model 1) included sex (male, female), race (black, white), study center (Birmingham, Chicago, Minneapolis, Oakland), year 0 age (continuous), and total energy (continuous). The model was further adjusted for smoking

status (current/ never/former), educational attainment, and physical activity (model 2). To investigate BMI and waist circumference as potential intermediaries between dietary patterns and endothelial function, we included these variables in a subsequent model (model 3).

We used the PC version (9.2) of the Statistical Analysis System (SAS, Cary, NC).

Results

Baseline characteristics

Age, white race, and educational attainment were positively associated with the *A Priori* Diet Quality Score and the FV pattern and negatively related to the meat dietary pattern (Table 1). Total energy decreased across quintiles of the *A Priori* Diet Quality Score and increased both in the meat and in the FV dietary patterns. People at higher levels of the *A Priori* Diet Quality Score and FV dietary pattern were less likely to smoke and had a lower waist circumference; the reverse was true for people scoring high on the meat dietary pattern. BMI decreased across quintiles of the *A Priori* Diet Quality Score and FV dietary pattern and was not significantly associated with the meat dietary pattern. Physical activity increased across quintiles of all three dietary patterns.

Unadjusted concentrations of E-selectin, P-selectin, and sICAM-1 were all lower at higher values of the *A Priori* Diet Quality Score and the FV pattern and higher at higher values of the meat dietary pattern. VCAM showed a reverse pattern, being positively related to the *A Priori* Diet Quality Score and the FV pattern, but inversely related to the meat pattern.

Tracking correlation coefficients between year 7 and 15 were 0.57 for P-selectin, 0.77 for E-selectin, 0.59 for sICAM-1, and 0.70 for VCAM. Correlations were 0.39 between E-selectin and P-selectin , 0.44 between E-selectin and sICAM-1, 0.26 between P-selectin and sICAM, and lower than 0.2 for all other combinations.

Dietary patterns and cellular adhesion molecules

In each multivariable model (Table 2), all three dietary patterns were associated with E-selectin. A strong association was seen with the meat dietary pattern (p_{trend} <0.001). In model 2, the mean E-selectin was 3.9 ng/mL higher in the highest meat dietary pattern quintile compared to the lowest. This was an effect size of 27% (3.9/13.7 ng/mL) of an SD.

P-selectin was inversely associated with the *A Priori* Diet Quality Score (p_{trend} 0.004) and positively with the meat dietary pattern (p_{trend} 0.02). The strongest association between P-selectin and diet was with the meat dietary pattern. The mean P-selectin was 4.1 ng/mL higher in the highest compared to the lowest meat dietary pattern quintile. This was an effect size of 37% (4.1/11.2 ng/mL) of an SD. P-selectin was not significantly associated with the FV dietary pattern.

All three dietary patterns were associated with sICAM-1. The *A Priori* Diet Quality Score was strongly inversely associated with sICAM-1(p_{trend} <0.001). The mean sICAM-1 was

15.1 ng/mL lower in the highest vs. the lowest *A Priori* Diet Quality Score quintile. This was an effect size of 34% of an SD (15.1/44.7 ng/mL) for sICAM-1.

VCAM was inversely associated with the *A Priori* Diet Quality Score (p_{trend} 0.006). The mean VCAM was 45.1 ng/mL lower in the highest vs. the lowest *A Priori* Diet Quality Score quintile. This was an effect size of 26% of an SD (45.1/170.3 ng/mL) for VCAM.

Further adjustment for BMI and waist (model 3) gave qualitatively similar results. Adjustment for plasma lipids (cholesterol, high-density lipoprotein and triglycerides) and measures of glucose metabolism (HOMA, glucose and insulin) did not substantively change the estimates shown in Model 3 of the association of diet with any of the CAMs (data not shown).

In a secondary analysis we examined associations of dietary patterns and CAMs at year 7 (Supplemental table 2). Cross-sectional associations were generally weaker than the longitudinal analysis presented in Table 3 and in some cases did not reach statistical significance. Cross-sectional associations of dietary patterns formed exclusively from year 7 data with the CAMs were similar to findings in Supplementary Table 1 for the *A Priori* Diet Quality Score, but were somewhat weaker for the two principal components patterns (data not shown).

Because the associations with the CAMs at year 15 tended to be stronger than the corresponding associations with CAMs at year 7, we looked at predicting evolution of the CAMs, using the full adjustment of model 3. Dependent variables were the year 15 CAM concentrations, covarying the year 7 CAM concentrations. For the *A Priori* Diet Quality Score, these associations were in the expected direction, that is better diet predicted less increase in each CAM, but p-values were generally not significant (E-selectin n = 1941, t = − 1.83, p = 0.07; P-selectin n = 2545, t = −1.56, p = 0.12; sICAM-1: n = 1698, t = −0.66, p = 0.51; VCAM n = 2580, t = −2.04, p = 0.04).

Discussion

We showed that CAMs are related longitudinally to dietary patterns. The *A Priori* Diet Quality Score was inversely related to E-selectin, P-selectin, sICAM-1, and VCAM. Using PCA, we identified an FV and a meat dietary pattern, which were, respectively, positively and inversely correlated with the *A Priori* Diet Quality Score. The FV dietary pattern was inversely associated with E-selectin and sICAM-1 but not with P-selectin and VCAM. The meat dietary pattern was positively associated with E-selectin, P-selectin, and sICAM-1, but not with VCAM. Although CAMs are related to adiposity, blood lipids, and insulin resistance, adjustment for the year 7 values of these variables did not suggest mediation of the diet-CAM associations.

Previous studies investigated cross-sectional associations of PCA-derived dietary patterns with CAMs. Nettleton et al. found that sICAM-1 was inversely associated with a “whole grain and fruit” pattern and positively related to a “bean, tomatoes and refined grain” pattern. “Fats and processed meats” and “vegetables and fish” patterns were not associated with sICAM-1, and E-selectin was not associated with any of the dietary patterns (8).

Similarly, Lopez-Garcia found that E-selectin, sICAM-1, and VCAM were positively associated with a PCA-derived Western diet. A prudent diet was only inversely associated with E-selectin (7). Fung et al. compared several diet quality scores and found E-selectin was inversely associated with all diet quality scores. sICAM-1 was inversely associated with the Alternate Healthy Eating Index (AHEI)(18) and Alternate Mediterranean Diet Index (aMED), and VCAM was only inversely associated to aMED (9).

This suggests that including different nutrients or food groups or different weightings of food groups included in the dietary patterns may affect the strength of the diet pattern associations with circulating markers of endothelial dysfunction. Diet quality scores are a stable characteristic compared to food groups or nutrients and are therefore a useful approach to study relations with CAMs. Although the findings are robust and in expected directions, there are differences in the strength of the associations of the CAMs and the three dietary patterns. All three dietary patterns were created using the same food groups, but the weightings of the food groups differ between the two methods. The PCA approach weights each food group, normalized to its standard deviation. The *A Priori* Diet Quality Score first sorts food groups into beneficial, adverse, or neutral, then weights them by their quintile position in the intake distribution. The *A Priori* Diet Quality Score emphasized more beneficial food groups (n=20) than adverse food groups (n=13). In terms of the *a priori* ratings of food groups as beneficial or adverse, the FV pattern emphasized the beneficial groups, whereas the meat dietary pattern emphasized the adverse food groups.

Our study sample was relatively young (mean age 32 at year 7, and 40 in year 15), and had lower concentrations of CAMs compared to previous studies (7-9), which could in part explain why our cross-sectional analysis showed weaker associations than our longitudinal associations.

CAMs have an important role in the accumulation of circulating leukocytes at sites of injury, infection, and inflammation. This accumulation of leukocytes involves several steps (known as the leukocyte adhesion cascade) and cell types including T and B cells, monocytes and macrophages, dendritic cells, and natural killer cells. In the cascade, cells undergo tethering, rolling, activation, arrest, tight adhesion, and diapedesis. Unique combinations of endothelial adhesion molecules and chemokines direct tissue-specific migration of leukocytes and control the various steps in the cascade (19-21). For example, P and E-selectin are involved in the tethering, rolling, and activation of leukocytes. ICAM-1 facilitates monocyte/ macrophage migration and adherence to endothelial cells. VCAM facilitates macrophage uptake into the subintimal space. Together, the CAMs form an integrated and overlapping system for the transport of leukocytes into the vascular wall and have an active role in the development of atherosclerotic plaque (22).

Our study has several strengths. First, repeated measurements of diet averaged for analysis may increase the reliability of our data. Second, because of the large CARDIA sample and extensive data we could adjust for important confounding variables. Third, our study included two primary methods to create dietary patterns. The *A Priori* Diet Quality Score is based on current judgment whereas the PCA patterns are based on correlations among food groups, as consumed by the participants. Fourth, repeated measurements of cellular adhesion

molecules allowed us to investigate associations of dietary patterns with these markers both cross-sectionally and longitudinally.

Our study also has limitations. Although we accounted for many possible confounders, as in every observational study, we cannot rule out residual confounding. In conclusion, both an *a priori* dietary score and *a posteriori* dietary patterns were related to endothelial function and support protective effects of a prudent dietary pattern high in fruits and vegetables and low in red meats, processed meats, and refined grains on health of the endothelium. The association of higher diet quality with biomarkers of endothelial function should be considered as a possible pathway through which diet may affect the development of cardiovascular disease.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1

Characteristics of study sample (mean (SD)) according to quintiles of averaged year 0/7 dietary pattern scores[1,2]

		***A Priori* Diet Quality Score**			**FV dietary pattern[4,5]**			**Meat dietary pattern [4,6]**		
		Q1	**Q3**	**Q5**	**Q1**	**Q3**	**Q5**	**Q1**	**Q3**	**Q5**
Dietary pattern score		48.2 (3.9)	62.9 (1.9)	81.2 (4.9)	−1.0 (0.2)	−0.2 (0.1)	1.3 (0.8)	−1.0 (0.2)	−0.2 (0.1)	1.5 (0.7)
Age (y)		23.4 (3.8)	25.0 (3.6)	26.3 (2.9)	24.1 (3.9)	25.2 (3.5)	25.7 (3.3)	25.7 (3.4)	25.1 (3.6)	24.2 (3.7)
Female (%)		46.7	52.6	65.7	60.1	55.5	48.3	84.9	53.9	20.7
White (%)		20.9	45.7	87.7	22.4	57.0	73.4	74.5	54.0	28.9
Current smoker (%)		34.0	29.0	16.3	35.0	26.5	19.4	14.5	25.5	46.6
Education attained (years)		14.1 (2.2)	15.3 (2.5)	16.9 (2.3)	14.2 (2.2)	15.7 (2.5)	16.3 (2.6)	16.4 (2.4)	15.7 (2.6)	14.1 (2.3)
Physical activity (exercise units)		321.8 (248.0)	362.8 (241.4)	467.3 (244.5)	269.9 (209.1)	356.8 (219.7)	505.1 (269.2)	372.1 (209.4)	354.1 (239.8)	465.7 (275.7)
Mean total energy (kcal/day)		3149 (1275.7)	2845.1 (1219.4)	2520.6 (924.2)	2346.9 (1032.4)	2624.7 (1011.2)	3383.5 (1267.5)	1743.1 (510.2)	2554.5 (517.9)	4582.3 (999.8)
Body Mass Index (kg/m^2)		26.1 (5.9)	25.9 (5.3)	24.2 (4.2)	26.4 (5.9)	25.6 (5.2)	24.9 (4.8)	24.7 (5.0)	25.9 (5.6)	25.3 (4.8)
Waist circumference (cm)		82.3 (13.1)	81.6 (12.1)	76.9 (10.1)	81.8 (12.9)	80.7 (12.0)	80.0 (11.8)	75.8 (10.9)	81.8 (12.4)	83.0 (11.5)
E-selectin, year 7	(n=3028)	36.8 (15.2)	34.5 (14.6)	29.5 (13.4)	36.1 (15.6)	33.7 (14.4)	31.7 (13.8)	29.1 (13.0)	34.1 (14.6)	38.6 (15.9)
E-selectin, year 15	(n=2789)	38.7 (14.8)	36.0 (13.3)	30.4 (12.2)	37.6 (14.5)	35.6 (13.9)	32.4 (12.5)	31.0 (13.2)	35.9 (14.2)	38.9 (13.9)
P-selectin, year 7	(n=3818)	29.7 (8.8)	28.5 (8.8)	26.7 (8.6)	29.3 (9.8)	28.5 (9.1)	28.0 (9.0)	25.6 (7.6)	28.9 (9.2)	31.9 (10.4)
P-selectin, year 15	(n=2947)	38.3 (12.0)	36.5 (10.2)	34.3 (10.5)	37.4 (10.7)	37.2 (12.3)	35.9 (11.1)	34.7 (9.9)	36.9 (11.2)	39.4 (12.4)
sICAM-1, year 7	(n=2538)	154.2 (32.2)	144.0 (34.1)	126.9 (26.8)	153.4 (32.7)	140.4 (34.6)	133.6 (30.7)	131.6 (31.0)	141.7 (30.1)	153.2 (34.1)
sICAM-1, year l5	(n=2911)	167.1 (49.7)	158.5 (48.1)	137.1 (31.5)	168.4 (50.8)	153.8 (45.3)	144.9 (35.2)	143.3 (37.9)	157.0 (48.9)	163.8 (41.5)
VCAM, year 7	(n=3809)	513.6 (202.7)	516.6 (157.2)	552.7 (160.7)	502.4 (170.5)	517.9 (156.4)	544.2 (168.6)	549.3 (164.0)	527.8 (163.5)	512.3 (183.4)
VCAM, year 15	(n=2998)	514.6 (210.8)	512.7 (151.5)	540.0 (163.6)	511.1 (195.7)	519.4 (158.5)	543.8 (170.8)	539.2 (154.9)	535.7 (178.7)	514.2 (196.7)

sICAM-1 soluble intercellular adhesion molecule 1, VCAM vascular cellular adhesion molecule

3 Trend across *A* Priori Diet Quality Score significant at <0.05 for all variables except VCAM year 7 (p-value 0.29)

[1] Data presented were averaged (year 0/7), except education (maximum attained over follow-up) and cellular adhesion molecules (as marked). N=3818 for all non CAM variables.

[2] Tests for trend of continuous variables were based on general linear regression with averaged year 0/7 dietary pattern as continuous independent variable adjusted for race sex center and age. Chi-square tests were used for categorical variables across all 5 levels of dietary pattern variables.

[4] Meat dietary pattern diet and FV dietary pattern are principal components, centered on zero with a standard deviation of 1.0.

[5] Trend FV dietary pattern significant at <0.05 for all variables except VCAM year 7 (p-value 0.48) and VCAM year 15 (p-value 0.64)

[6]Trends across Meat dietary pattern significant at <0.05 for all variables except waist (p-value 0.99), VCAM year 7 (p-value 0.35) and VCAM year 15 (p-value 0.15)

Table 2

Estimates (SE) of year 15 soluble adhesion molecules per quintile of averaged year 0/7 dietary pattern

		Quintile of Dietary Pattern Consumption					
		1	2	3	4	5	Ptrend[1]
A Priori Diet Quality Score	E selectin year 15 (35.1 (13.7))	446	514	576	643	639	
	model 1	0	−0.5 (0.8)	−1.3 (0.9)	−1.8 (0.9)	−4.2 (1.0)	<0.001
	model 2	0	−0.3 (0.8)	−0.7 (0.9)	−0.7 (0.9)	−2.4 (1.0)	0.02
	model 3	0	−0.5 (0.8)	−0.8 (0.8)	−0.6 (0.9)	−1.8 (1.0)	0.08
	P selectin year 15 (36.8 (11.2))	471	537	611	682	646	
	model 1	0	−0.4 (0.7)	−2.0 (0.7)	−1.2 (0.7)	−3.4 (0.8)	<0.001
	model 2	0	−0.3 (0.7)	−1.7 (0.7)	−0.6 (0.7)	−2.6 (0.8)	0.004
	model 3	0	−0.4 (0.7)	−1.7 (0.7)	−0.6 (0.7)	−2.4 (0.8)	0.009
	sICAM-1 year 15 (154.7 (44.7))	464	531	603	674	639	
	model 1	0	−1.2 (2.7)	−5.6 (2.7)	−9.5 (2.8)	−21.2 (3.1)	<0.001
	model 2	0	−0.9 (2.6)	−4.3 (2.7)	−5.9 (2.8)	−15.1 (3.1)	<0.001
	model 3	0	−1.4 (2.6)	−4.3 (2.6)	−5.5 (2.7)	−12.9 (3.1)	<0.001
	VCAM year 15 (525.8 (170.3))	417	541	618	657	665	
	model 1	0	−19.3 (10.1)	−32.4 (10.1)	−18.7 (10.6)	−45.4 (11.6)	0.002
	model 2	0	−19.4 (10.2)	−32.1 (10.3)	−18.9 (11.0)	−45.1 (12.4)	0.006
	model 3	0	−18.9 (10.2)	−31.9 (10.3)	−18.7 (11.0)	−45.5 (12.4)	0.005
FV dietary pattern	E selectin year 15	495	551	576	583	584	
	model 1	0	−0.8 (0.8)	−0.7 (0.8)	−1.3 (0.9)	−3.5 (0.9)	<0.001
	model 2	0	0.0 (0.8)	0.4 (0.8)	0.4 (0.9)	−1.3 (1.0)	0.03
	model 3	0	0.0 (0.8)	0.5 (0.8)	0.5 (0.9)	−1.2 (1.0)	0.02
	P selectin year 15	524	585	600	619	619	
	model 1	0	−0.4 (0.7)	−0.6 (0.7)	−1.5 (0.7)	−2.2 (0.8)	0.003
	model 2	0	0.1 (0.7)	0.1 (0.7)	−0.4 (0.7)	−0.8 (0.8)	0.28
	model 3	0	0.1 (0.7)	0.2 (0.7)	−0.3 (0.7)	−0.8 (0.8)	0.26
	sICAM-1 year 15	520	574	594	617	606	
	model 1	0	−5.9 (2.6)	−10.2 (2.7)	−14.7 (2.8)	−18.5 (3.0)	<0.001
	model 2	0	−2.2 (2.5)	−4.5 (2.6)	−5.8 (2.8)	−7.5 (3.1)	0.02
	model 3	0	−2.2 (2.5)	−4.0 (2.6)	−5.3 (2.7)	−7.1 (3.0)	0.01
	VCAM year 15	547	609	595	627	620	
	model 1	0	−19.8 (9.9)	−30.7 (10.3)	−26.0 (10.8)	−25.0 (11.6)	0.18
	model 2	0	−19.7 (9.9)	−30.7 (10.5)	−26.1 (11.2)	−24.8 (12.2)	0.25
	model 3	0	−19.5 (10.0)	−30.5 (10.5)	−25.8 (11.2)	−24.6 (12.2)	0.26
	E selectin year 15	570	594	503	561	461	
	model 1	0	1.3 (1.0)	3.0 (1.2)	5.5 (1.3)	6.2 (1.5)	<0.001
	model 2	0	0.2 (1.0)	1.5 (1.2)	3.6 (1.4)	3.9 (1.5)	<0.001
	model 3	0	0.7 (1.0)	1.9 (1.2)	3.5 (1.3)	3.3 (1.5)	0.001
	P selectin year 15	600	633	637	693	484	

		Quintile of Dietary Pattern Consumption					
		1	2	3	4	5	Ptrend[1]
Meat dietary pattern	model 1	0	2.4 (0.8)	3.8 (1.0)	5.3 (1.1)	5.7 (1.2)	<0.001
	model 2	0	1.7 (0.8)	2.9 (1.0)	3.9 (1.1)	4.1 (1.2)	0.02
	model 3	0	1.9 (0.8)	3.0 (1.0)	3.9 (1.1)	3.9 (1.2)	0.02
	sICAM-1 year 15	599	625	634	581	472	
	model 1	0	4.3 (3.3)	12.7 (3.8)	21.5 (4.4)	26.7 (4.8)	<0.001
	model 2	0	−1.9 (3.2)	3.9 (3.7)	9.0 (4.3)	11.9 (4.8)	0.02
	model 3	0	−0.5 (3.1)	4.9 (3.7)	8.5 (4.2)	9.8 (4.7)	0.04
	VCAM year 15	641	641	635	570	511	
	model 1	0	10.1 (12.2)	−6.8 (14.4)	14.8 (16.3)	7.3 (18.2)	0.73
	model 2	0	10.5 (12.3)	−6.5 (14.6)	16.2 (16.7)	7.3 (18.8)	0.67
	model 3	0	9.9 (12.3)	−7.2 (14.7)	15.7 (16.7)	7.0 (18.8)	0.67

sICAM-1 soluble intercellular adhesion molecule 1, VCAM vascular cellular adhesion molecule 1

Model 1: covariates include, race, sex, center, age, energy

Model 2: model 1 plus smoking status, educational attainment and physical activity

Model 3: model 2 plus BMI and waist

[1] P-value for trend based on multivariate adjusted regression analysis with dietary pattern as a continuous value