

# Dietary Patterns and Markers of Systemic Inflammation among Iranian Women<sup>1</sup>

Ahmad Esmailzadeh,<sup>2,3\*</sup> Masoud Kimiagar,<sup>4</sup> Yadollah Mehrabi,<sup>5</sup> Leila Azadbakht,<sup>2,3</sup> Frank B. Hu,<sup>6,7</sup> and Walter C. Willett<sup>6,7</sup>

<sup>2</sup>Department of Nutrition, School of Health and <sup>3</sup>Nutrition Research Center, Isfahan University of Medical Sciences, Isfahan PO Box 81745, Iran; <sup>4</sup>Department of Human Nutrition, School of Nutrition and Food Science and <sup>5</sup>School of Public Health, Shaheed Beheshti University of Medical Sciences, Tehran PO Box 19826-19573, Iran; and <sup>6</sup>Department of Nutrition and <sup>7</sup>Department of Epidemiology, Harvard School of Public Health, Boston, MA 02115

## Abstract

Few studies have examined the contribution of major dietary patterns to markers of systemic inflammation. This study was conducted to evaluate the association of major dietary patterns with markers of systemic inflammation among Iranian women. In a cross-sectional study of 486 healthy women aged 40–60 y, we assessed usual dietary intakes by means of an FFQ. Dietary patterns were identified by factor analysis. Anthropometric measurements were made and blood samples from fasting were taken for measuring inflammatory markers. The healthy pattern (high in fruits, vegetables, tomato, poultry, legumes, tea, fruit juices, and whole grains) was inversely related to plasma concentrations of C-reactive protein (CRP) ( $\beta = -0.09$ ,  $P < 0.001$ ), E-selectin ( $\beta = -0.07$ ,  $P < 0.05$ ), and soluble vascular cell adhesion molecule-1 (sVCAM-1) ( $\beta = -0.08$ ,  $P < 0.001$ ) after control for potential confounders; with further adjustment for BMI and waist circumference (WC), the associations remained significant for CRP ( $\beta = -0.05$ ,  $P < 0.05$ ) and sVCAM-1 ( $\beta = -0.04$ ,  $P < 0.05$ ). In contrast, the western pattern score (high in refined grains, red meat, butter, processed meat, high-fat dairy, sweets and desserts, pizza, potato, eggs, hydrogenated fats, and soft drinks) was positively related to CRP ( $\beta = 0.08$ ,  $P < 0.001$ ), serum amyloid A (SAA) ( $\beta = 0.11$ ,  $P < 0.05$ ), IL-6 ( $\beta = 0.09$ ,  $P < 0.001$ ), soluble intercellular adhesion molecule-1 ( $\beta = 0.05$ ,  $P < 0.05$ ), and sVCAM-1 concentrations ( $\beta = 0.07$ ,  $P < 0.05$ ). However, after additional control for BMI and WC, the associations remained significant only for SAA ( $\beta = 0.06$ ,  $P < 0.05$ ) and IL-6 ( $\beta = 0.07$ ,  $P < 0.001$ ). The traditional dietary pattern (high in refined grains, potato, tea, whole grains, hydrogenated fats, legumes, and casserole) was positively associated with the plasma IL-6 concentration ( $\beta = 0.04$ ,  $P < 0.05$ ) when we controlled for confounders including BMI and WC. The findings suggest an independent association between major dietary patterns and plasma concentrations of markers of inflammation. *J. Nutr.* 137: 992–998, 2007.

## Introduction

Current evidence suggests elevated plasma levels of inflammatory markers are risk factors for many chronic diseases, including obesity (1,2), diabetes (3), metabolic syndrome (4), and many types of cardiovascular diseases (5,6). Levels of inflammatory markers have also been correlated with various cardiovascular risk factors, such as smoking (7), hypertension (8), low HDL-cholesterol (9), and dyslipidemia (10). Factors affecting systemic inflammation markers are largely unknown. Although several genetic and environmental determinants have been established (11–14), few studies have examined the association of diet with markers of systemic inflammation (15–17); most of them have focused on foods (18,19) and nutrients (20,21). Comparatively little emphasis has been placed on the specific contribution of dietary patterns (22–24) that provide a broad

concept of diet including both food and nutrient composition (25). Although the dietary pattern approach has received much attention over recent years in relation to chronic diseases, few studies have assessed whether its effects are mediated through changes in plasma concentrations of inflammatory markers. To our knowledge, no study has assessed this association in an Asian population whose dietary patterns and plasma levels of inflammatory markers may be different from those in western countries. In this study, our main objective was to assess the association between major dietary patterns and markers of systemic inflammation in a group of Tehrani female teachers.

## Subjects and Methods

**Participants.** This cross-sectional study was conducted among a representative sample of Tehrani female teachers aged 40–60 y selected by a multistage cluster random sampling method. A random sample of 583 female teachers were invited to participate in this study and 521 women agreed. Participants with a prior history of cardiovascular disease, diabetes, cancer, and stroke were excluded because of possible changes in

<sup>1</sup> Supported by the National Nutrition and Food Technology Research Institute, Shaheed Beheshti University of Medical Sciences.

\* To whom correspondence should be addressed. E-mail: esmailzadeh@hlth.mui.ac.ir.

diet. We also excluded women who left >70 items blank on the FFQ, who reported a total daily energy intake outside the range of 800–4200 kcal (3344–17556 kJ), and those taking medications that would affect plasma lipoproteins, blood pressure, and carbohydrate metabolism. After these exclusions, 486 women remained for the present analysis. This study was approved by the research council of the National Nutrition and Food Technology Research Institute, Shaheed Beheshti University of Medical Sciences, and informed written consent was obtained from each participant.

**Assessment of dietary intake.** Usual dietary intake was assessed using a validated 168-item semiquantitative FFQ. A trained dietitian administered all the questionnaires. The FFQ consisted of a list of foods with standard serving sizes commonly consumed by Iranians. Participants were asked to report their frequency of consumption of a given serving of each food item during the previous year on a daily (e.g. bread), weekly (e.g. rice, meat), or monthly (e.g. fish) basis. The reported frequency for each food item was then converted to a daily intake. Portion sizes of consumed foods were converted to g using household measures (26). Total energy intake was calculated by summing energy intakes from all foods. To determine the nutrient compositions of Iranian foods, we used an Iranian food composition table (27) in conjunction with USDA food composition data (28). Foods from FFQ were classified into 41 food groups on the basis of nutrient profiles or culinary usage (Appendix 1). Foods that did not fit into any of the groups or that may represent distinctive dietary behaviors were left as individual categories and entered as separate food groups. A previous validation study (29) of this FFQ among 132 randomly chosen participants (not included in this study) revealed correlations between dietary intakes assessed by similar FFQ and multiple days of 24-h food recalls completed during the year ( $r = 0.3-0.8$ ;  $P < 0.05$ ).

**Assessment of biomarkers.** A blood sample was drawn between 0700 and 0900 into vacutainer tubes from all study participants after >12 h overnight fasting. Blood samples, collected into tubes containing 0.1% EDTA, were taken in a sitting position according to a standard protocol and centrifuged within 30–45 min of collection. Blood was centrifuged to separate the plasma from the buffy coat and red blood cells. Plasma was frozen at  $-70^{\circ}\text{C}$  until analysis. C-reactive protein (CRP)<sup>8</sup> concentrations were measured using an ultrasensitive latex-enhanced immunoturbidimetric assay (Randox). Concentrations of serum amyloid A (SAA) and plasma E-selectin, soluble intercellular adhesion molecule-1 (sICAM-1), and soluble vascular cell adhesion molecule-1 (sVCAM-1) were measured by commercially available ELISA and standards (Biosource International and Bender MedSystems). Plasma concentrations of TNF- $\alpha$  and IL-6 were assayed by ELISA kits (Bender MedSystems). Five percent of samples were analyzed in duplicate to ensure the reproducibility of results. The sensitivities of the assays for sICAM-1, sVCAM-1, and E-selectin were 0.6, 2.3, and 0.3  $\mu\text{g/L}$ , respectively, and there was no cross-reactivity with other adhesion molecules. The sensitivities of the assays for TNF- $\alpha$ , IL-6, SAA, and CRP were 1.8, 1.1, 0.9  $\mu\text{g/L}$ , and 0.4 mg/L, respectively. Inter- and intra-assay CV for all markers were <10%. Plasma lipid concentrations were measured using standard methods (30).

**Assessment of other variables.** Weight was measured using digital scales and recorded to the nearest 100 g while the participants were minimally clothed without shoes. Height was measured in a standing position, without shoes, using a tape measure while the shoulders were in a normal position. BMI was calculated as weight in kg divided by height in  $\text{m}^2$ . Waist circumference (WC) was measured at the narrowest level and that of the hip at the maximum level over light clothing using an unstretched tape measure, without any pressure to body surface; measurements were recorded to the nearest 0.1 cm. Data on physical activity were obtained using participants' oral responses to an interview-

based International Physical Activity Questionnaire and expressed as metabolic equivalent h/wk (MET-h/wk)(31). This questionnaire includes questions in 5 activity domains: job-related physical activity; transportation physical activity; activities for housework and house maintenance; recreation, sport, and leisure-time physical activity; and time spent sitting. We asked participants to think about all the vigorous and moderate activities they engaged in during the last 7 d, considering times spent for these activities. Additional covariate information regarding age, smoking habits, menopausal status, medical history, and current use of medications was obtained using questionnaires. Blood pressures were assessed according to a standard protocol (30).

**Statistical methods.** To identify major dietary patterns based on the 41 food groups, we used principal component analysis with the factors rotated by orthogonal transformation. The natural interpretation of the factors in conjunction with Eigen values (>1) and Scree test (32) determined whether a factor should be retained. The derived factors (dietary patterns) were labeled on the basis of our interpretation of the data as well as on prior literature. The factor score for each pattern was calculated by summing intakes of food groups weighted by their factor loadings (32) and each subject received a factor score for each identified pattern.

Cut-points for quintiles of dietary pattern scores were calculated and participants were categorized based on quintile cut-points. We used 1-way ANOVA with Tukey post hoc comparisons for quantitative variables and chi-square tests for qualitative variables to identify significant differences across quintile categories of dietary pattern scores. We also determined age- and energy-adjusted means for dietary variables across quintiles and used analysis of covariance with Bonferroni correction to compare these means.

The distribution of inflammatory markers was highly skewed. Therefore, logarithmically transformed values of these markers were used in all analyses. Geometric means of inflammatory markers were computed using analysis of covariance in 3 different models. The first model was adjusted for age (y), physical activity (MET-h/wk), current estrogen use (yes or no), menopausal status (yes or no), family history of diabetes and stroke (yes or no), and energy intake (kcal) in the 2nd model. In a 3rd model, we controlled for BMI and WC.

We used multiple linear regression analysis to determine the association of dietary patterns with inflammatory markers. All models were adjusted for age (y), physical activity (MET-h/wk), cigarette smoking (yes or no), menopausal status (yes or no), current estrogen use (yes or no), family history of diabetes and stroke (yes or no), and energy intake (continuous). We further adjusted for BMI and WC to examine if the relation is mediated by obesity. All statistical analyses were performed using Statistical Package for Social Science (version 9.05).

## Results

We identified 3 major dietary patterns using factor analysis (Appendix 2): the healthy dietary pattern (high in fruits, vegetables, tomatoes, poultry, legumes, cruciferous and green leafy vegetables, tea, fruit juices, and whole grains); the western dietary pattern (high in refined grains, red meat, butter, processed meat, high-fat dairy products, sweets and desserts, pizza, potatoes, eggs, hydrogenated fats, and soft drinks and low in other vegetables and low-fat dairy products); and the traditional dietary pattern (high in refined grains, potato, tea, whole grains, hydrogenated fats, legumes, and casserole). These factors explained 24% of the variance.

Characteristics of the study participants across quintile categories of dietary patterns score are shown in Table 1. Age- and energy-adjusted means for dietary variables are also presented in this table. Compared with participants in the lower quintile, those in the upper quintile of the healthy dietary pattern had lower BMI, were more physically active, and were less likely to be obese. Conversely, those in the upper quintile of the western dietary pattern had higher BMI, were less likely to exercise, and had higher prevalence of obesity. Individuals in the upper quintile of traditional dietary pattern were older and slightly more physically

<sup>8</sup> Abbreviations used: CRP, C-reactive protein; MET-h/wk, metabolic equivalent h/wk; SAA, serum amyloid A; sICAM-1, soluble intercellular adhesion molecule-1; sVCAM-1, soluble vascular cell adhesion molecule-1; WC, waist circumference.

**TABLE 1** Characteristics and dietary intakes of study participants by quintile categories of dietary patterns scores<sup>1</sup>

|                               | Quintiles of healthy pattern score |                          |                          |                | Quintiles of western pattern score |                         |                          |                | Quintiles of traditional pattern score |                         |                          |                |
|-------------------------------|------------------------------------|--------------------------|--------------------------|----------------|------------------------------------|-------------------------|--------------------------|----------------|--|-------------------------|--------------------------|----------------|
|                               | 1 (lowest)                         | 3                        | 5 (highest)              | P <sup>2</sup> | 1 (lowest)                         | 3                       | 5 (highest)              | P <sup>2</sup> | 1 (lowest)                             | 3                       | 5 (highest)              | P <sup>2</sup> |
| <i>n</i>                      | 97                                 | 97                       | 97                       |                | 97                                 | 97                      | 97                       |                | 97                                     | 97                      | 97                       |                |
| Age, y                        | 49 ± 6                             | 50 ± 7                   | 48 ± 6                   | 0.18           | 47 ± 7                             | 51 ± 7 <sup>b</sup>     | 48 ± 6                   | <0.05          | 45 ± 8                                 | 53 ± 6 <sup>6</sup>     | 51 ± 7 <sup>6</sup>      | <0.01          |
| BMI, kg/m <sup>2</sup>        | 30.4 ± 3.4                         | 27.8 ± 3.9 <sup>a</sup>  | 25.7 ± 3.8 <sup>a</sup>  | <0.01          | 26.3 ± 3.7                         | 27.9 ± 4.1 <sup>a</sup> | 29.6 ± 3.6 <sup>a</sup>  | <0.01          | 28.3 ± 3.4                             | 27.1 ± 3.8 <sup>c</sup> | 27.9 ± 3.6               | <0.05          |
| Waist/hip ratio               | 0.91 ± 0.08                        | 0.89 ± 0.08              | 0.85 ± 0.05 <sup>a</sup> | <0.01          | 0.87 ± 0.08                        | 0.90 ± 0.05             | 0.93 ± 0.08 <sup>a</sup> | <0.01          | 0.89 ± 0.08                            | 0.87 ± 0.08             | 0.88 ± 0.08              | 0.19           |
| Physical activity, MET-h/wk   | 10.3 ± 9.1                         | 14.7 ± 11.2 <sup>a</sup> | 17.3 ± 10.8 <sup>a</sup> | <0.01          | 16.6 ± 11.1                        | 14.8 ± 9.7 <sup>a</sup> | 11.1 ± 10.2 <sup>a</sup> | <0.01          | 13.9 ± 10.4                            | 14.7 ± 11.1             | 15.6 ± 10.3 <sup>c</sup> | <0.05          |
| Family history of diabetes, % | 9                                  | 11                       | 11                       | <0.05          | 10                                 | 9                       | 10                       | 0.11           | 8                                      | 11                      | 10                       | <0.05          |
| Family history of stroke, %   | 1                                  | 1                        | 2                        | 0.74           | 1                                  | 1                       | 1                        | 0.89           | 1                                      | 0                       | 1                        | 0.83           |
| Current daily smokers, %      | 1                                  | 1                        | 0                        | 0.81           | 0                                  | 0                       | 1                        | 0.73           | 1                                      | 1                       | 0                        | 0.85           |
| Obese, <sup>3</sup> %         | 47                                 | 35                       | 20                       | <0.01          | 23                                 | 37                      | 44                       | <0.01          | 35                                     | 32                      | 31                       | <0.05          |
| Current estrogen use, %       | 24                                 | 26                       | 26                       | 0.09           | 23                                 | 27                      | 25                       | <0.05          | 27                                     | 27                      | 24                       | 0.07           |
| Dietary intakes               |                                    |                          |                          |                |                                    |                         |                          |                |  |                         |                          |                |
| Total energy, kcal/d          | 2675                               | 2341 <sup>a</sup>        | 2052 <sup>a</sup>        | <0.01          | 2133                               | 2512 <sup>a</sup>       | 2735 <sup>a</sup>        | <0.01          | 2519                                   | 2672                    | 2239 <sup>b</sup>        | <0.05          |
| <i>kJ/d</i>                   | 11182                              | 9785                     | 8577                     |                | 8916                               | 10500                   | 11432                    |                | 10529                                  | 11169                   | 9359                     |                |
| Carbohydrate, % total energy  | 59                                 | 58                       | 56 <sup>c</sup>          | <0.05          | 57                                 | 59                      | 58                       | <0.07          | 58                                     | 59                      | 59                       | 0.13           |
| Protein, % total energy       | 10                                 | 13 <sup>a</sup>          | 14 <sup>a</sup>          | <0.01          | 15                                 | 11 <sup>c</sup>         | 13                       | <0.05          | 13                                     | 14                      | 14                       | 0.09           |
| Fat, % total energy           | 31                                 | 29 <sup>c</sup>          | 28 <sup>c</sup>          | <0.05          | 28                                 | 30 <sup>c</sup>         | 31 <sup>c</sup>          | <0.05          | 29                                     | 27 <sup>b</sup>         | 27 <sup>b</sup>          | <0.05          |
| Cholesterol, mg/d             | 191                                | 179 <sup>b</sup>         | 150 <sup>b</sup>         | <0.05          | 142                                | 165 <sup>b</sup>        | 198 <sup>b</sup>         | <0.05          | 183                                    | 174                     | 180                      | 0.38           |
| Dietary fiber, g/d            | 12                                 | 15 <sup>b</sup>          | 19 <sup>b</sup>          | <0.01          | 18                                 | 13 <sup>a</sup>         | 9 <sup>a</sup>           | <0.01          | 14                                     | 12 <sup>b</sup>         | 16                       | <0.05          |
| Vitamin B-6, mg/d             | 0.7                                | 0.7                      | 1.1 <sup>a</sup>         | <0.01          | 1.2 <sup>a</sup>                   | 0.8                     | 0.7                      | <0.01          | 1.0                                    | 0.9                     | 1.2                      | 0.06           |
| Magnesium, mg/d               | 124                                | 149 <sup>a</sup>         | 171 <sup>a</sup>         | <0.01          | 182                                | 139 <sup>a</sup>        | 108 <sup>a</sup>         | <0.01          | 131                                    | 126                     | 137                      | 0.10           |

<sup>1</sup> Values are means ± SD unless indicated. Reported means for nutrients intake are adjusted for age and energy intake. Letters indicate differences within a pattern: <sup>a</sup> vs. other quintiles, *P* < 0.01, <sup>b</sup> vs. other quintiles, *P* < 0.05, <sup>c</sup> vs. quintile 1, *P* < 0.05.

<sup>2</sup> ANOVA for quantitative variables and chi-square for qualitative variables.

<sup>3</sup> Obese: BMI ≥ 30 kg/m<sup>2</sup>.

active and less likely to be obese compared with those in the lowest quintile. Distribution of current smokers and estrogen users across quintile categories of dietary patterns did not differ. Those in the upper category of the healthy dietary pattern had lower intakes of energy and cholesterol and higher intakes of vitamin B-6, magnesium, and fiber, whereas those in the top quintile of the western dietary pattern had higher intakes of energy and cholesterol and lower intake of vitamin B-6, magnesium, and fiber. Individuals in the upper quintile of the traditional dietary pattern had slightly lower energy intake than those in the lowest category, but their nutrient intakes were not significantly different in most cases (*P* > 0.05).

Multivariate-adjusted geometric means for plasma concentrations of markers of inflammation across quintiles of dietary patterns score are presented in Table 2. After controlling for age, the healthy dietary pattern score was inversely associated with plasma concentrations of CRP, TNF- $\alpha$ , sVCAM-1, and E-selectin. These associations remained significant even after additional control for other confounders. However, adjustment for BMI and WC attenuated all associations. In contrast to the healthy dietary pattern score, the western dietary pattern score was positively related to plasma concentrations of inflammatory markers. The relations were significant for CRP, sVCAM-1, sICAM-1, IL-6, and SAA after adjusting for age and other potential confounders. After additional control for BMI and WC, the associations with sVCAM-1 and sICAM-1 disappeared and that with CRP became marginally significant (*P* = 0.04). The traditional dietary pattern score was positively associated with TNF- $\alpha$  after controlling for age and other potential confounders. However, when we further controlled for BMI and WC, all associations were nonsignificant except for IL-6 and E-selectin (*P* < 0.05); those in the top category of traditional dietary pattern had higher plasma concentrations of these inflammatory markers.

The results of multiple linear regression models, which included major dietary pattern scores as independent and log-transformed values of inflammatory markers as dependent variables, are shown in Table 3. The healthy pattern score was inversely related to plasma concentrations of CRP, E-selectin, and sVCAM-1 after controlling for potential confounders except BMI and WC; with further adjustment for BMI and WC, the associations remained significant for CRP and sVCAM-1. The western pattern score was positively related to CRP, SAA, IL-6, sICAM-1, and sVCAM-1 levels; however, after additional control for BMI and WC, the associations remained significant only for SAA and IL-6. The traditional dietary pattern was positively associated with plasma levels of IL-6 when we controlled for confounders including BMI and WC.

## Discussion

We observed an inverse relation between the healthy dietary pattern and plasma concentrations of CRP, E-selectin, and sVCAM-1 and a positive relation between the western dietary pattern and levels of CRP, SAA, IL-6, sICAM-1, and sVCAM-1. After additional control for BMI and WC, the associations remained significant between the healthy dietary pattern and CRP and sVCAM-1 levels and between the western dietary pattern and SAA and IL-6 levels. This adjustment also revealed a significant association between traditional dietary pattern and IL-6. However, all  $\beta$  coefficients we found were low due to the use of log-transformed values of inflammatory markers.

A growing body of evidence supports a pivotal role for inflammation in atherosclerosis, whereas little information is available about the effects of diet, particularly dietary patterns, on inflammation. CRP, IL-6, and cell adhesion molecules like sICAM-1, sVCAM-1, and E-selectin are all important

**TABLE 2** Multivariate-adjusted geometric means of circulating inflammatory marker concentrations across quintile categories of dietary patterns score in Tehrani women<sup>1</sup>

| Inflammatory markers   | Quintiles of healthy pattern score |             |             |                | Quintiles of western pattern score |             |             |                | Quintiles of traditional pattern score |             |             |                |
|------------------------|------------------------------------|-------------|-------------|----------------|------------------------------------|-------------|-------------|----------------|--|-------------|-------------|----------------|
|                        | 1 (lowest)                         | 3           | 5 (highest) | P <sup>2</sup> | 1 (lowest)                         | 3           | 5 (highest) | P <sup>2</sup> | 1 (lowest)                             | 3           | 5 (highest) | P <sup>2</sup> |
| <i>n</i>               | 97                                 | 97          | 97          |                | 97                                 | 97          | 97          |                | 97                                     | 97          | 97          |                |
| CRP, mg/L              |                                    |             |             |                |                                    |             |             |                |  |             |             |                |
| Model I <sup>3</sup>   | 2.6 ± 2.1                          | 2.1 ± 3.4   | 1.5 ± 2.2   | <0.01          | 1.7 ± 2.6                          | 2.1 ± 2.9   | 2.8 ± 2.5   | <0.01          | 2.2 ± 2.7                              | 2.4 ± 2.4   | 2.1 ± 2.2   | 0.47           |
| Model II <sup>4</sup>  | 2.4 ± 1.5                          | 2.0 ± 2.3   | 1.7 ± 1.8   | <0.01          | 1.8 ± 2.3                          | 2.1 ± 2.6   | 2.6 ± 2.2   | <0.01          | 2.1 ± 2.5                              | 2.2 ± 2.2   | 2.3 ± 2.1   | 0.81           |
| Model III <sup>5</sup> | 2.2 ± 1.2                          | 1.8 ± 1.8   | 1.9 ± 1.3   | <0.05          | 2.0 ± 2.2                          | 2.0 ± 2.3   | 2.3 ± 2.0   | <0.05          | 2.1 ± 2.4                              | 2.3 ± 2.2   | 2.2 ± 2.2   | 0.79           |
| TNF-α, ng/L            |                                    |             |             |                |                                    |             |             |                |  |             |             |                |
| Model I                | 5.3 ± 2.6                          | 4.7 ± 2.3   | 4.1 ± 1.8   | <0.01          | 4.7 ± 2.1                          | 4.8 ± 2.9   | 4.6 ± 2.8   | 0.23           | 5.1 ± 2.5                              | 4.5 ± 2.3   | 4.8 ± 2.6   | <0.05          |
| Model II               | 5.0 ± 2.5                          | 4.8 ± 2.1   | 4.4 ± 1.7   | <0.01          | 4.8 ± 2.0                          | 4.8 ± 2.9   | 4.7 ± 2.7   | 0.16           | 5.0 ± 2.4                              | 4.5 ± 2.2   | 4.9 ± 2.4   | <0.05          |
| Model III              | 4.7 ± 2.5                          | 4.7 ± 2.0   | 4.6 ± 1.7   | 0.08           | 5.0 ± 1.8                          | 4.7 ± 2.8   | 4.3 ± 2.5   | <0.05          | 4.9 ± 2.3                              | 4.7 ± 2.0   | 5.0 ± 2.2   | 0.09           |
| SAA, mg/L              |                                    |             |             |                |                                    |             |             |                |  |             |             |                |
| Model I                | 4.7 ± 3.3                          | 4.9 ± 3.2   | 4.8 ± 2.9   | 0.45           | 4.0 ± 3.0                          | 4.8 ± 2.7   | 5.6 ± 3.2   | <0.01          | 5.1 ± 3.2                              | 4.8 ± 3.3   | 4.5 ± 2.8   | <0.05          |
| Model II               | 4.6 ± 3.0                          | 4.8 ± 3.0   | 4.8 ± 2.8   | 0.23           | 4.0 ± 2.9                          | 4.7 ± 2.7   | 5.6 ± 3.0   | <0.01          | 4.9 ± 3.0                              | 4.6 ± 3.1   | 4.7 ± 3.0   | 0.29           |
| Model III              | 4.5 ± 2.9                          | 4.7 ± 2.8   | 4.7 ± 2.7   | 0.18           | 4.2 ± 3.0                          | 4.7 ± 2.6   | 5.5 ± 3.0   | <0.01          | 4.8 ± 3.1                              | 4.7 ± 3.0   | 4.8 ± 2.9   | 0.56           |
| IL-6, ng/L             |                                    |             |             |                |                                    |             |             |                |  |             |             |                |
| Model I                | 1.8 ± 1.9                          | 1.8 ± 1.6   | 1.7 ± 2.1   | 0.27           | 1.4 ± 1.9                          | 1.9 ± 2.3   | 2.4 ± 2.1   | <0.01          | 1.9 ± 2.0                              | 2.1 ± 2.5   | 2.0 ± 1.8   | 0.47           |
| Model II               | 1.8 ± 1.8                          | 1.7 ± 1.5   | 1.7 ± 1.9   | 0.19           | 1.4 ± 1.8                          | 1.8 ± 2.1   | 2.3 ± 2.0   | <0.01          | 1.8 ± 1.9                              | 2.0 ± 2.3   | 2.1 ± 1.8   | 0.21           |
| Model III              | 1.6 ± 1.7                          | 1.8 ± 1.5   | 1.8 ± 1.8   | 0.16           | 1.4 ± 1.8                          | 1.8 ± 2.0   | 2.2 ± 2.0   | <0.01          | 1.7 ± 1.9                              | 2.2 ± 2.1   | 2.3 ± 1.7   | <0.05          |
| E-selectin, ng/L       |                                    |             |             |                |                                    |             |             |                |  |             |             |                |
| Model I                | 54.1 ± 19.7                        | 49.8 ± 15.9 | 43.3 ± 17.2 | <0.01          | 48.5 ± 16.7                        | 49.3 ± 17.3 | 49.9 ± 14.8 | 0.75           | 47.8 ± 18.3                            | 49.4 ± 15.9 | 48.9 ± 16.5 | 0.55           |
| Model II               | 52.4 ± 18.1                        | 48.7 ± 15.3 | 44.9 ± 16.8 | <0.01          | 49.1 ± 16.1                        | 49.0 ± 16.9 | 49.2 ± 15.3 | 0.70           | 47.1 ± 18.9                            | 49.0 ± 15.5 | 49.3 ± 15.9 | 0.51           |
| Model III              | 49.7 ± 18.5                        | 46.9 ± 15.0 | 46.8 ± 16.5 | <0.05          | 50.3 ± 15.8                        | 48.6 ± 16.8 | 47.9 ± 15.1 | 0.29           | 46.5 ± 18.5                            | 49.9 ± 15.3 | 52.9 ± 15.8 | <0.05          |
| sICAM-1, μg/L          |                                    |             |             |                |                                    |             |             |                |  |             |             |                |
| Model I                | 249 ± 58                           | 248 ± 44    | 244 ± 51    | 0.23           | 237 ± 55                           | 249 ± 63    | 254 ± 56    | <0.05          | 248 ± 59                               | 251 ± 61    | 250 ± 49    | 0.73           |
| Model II               | 245 ± 56                           | 249 ± 44    | 246 ± 50    | 0.29           | 239 ± 54                           | 248 ± 65    | 251 ± 54    | <0.05          | 248 ± 55                               | 249 ± 58    | 250 ± 48    | 0.81           |
| Model III              | 241 ± 55                           | 247 ± 43    | 250 ± 50    | 0.10           | 245 ± 57                           | 243 ± 61    | 244 ± 55    | 0.59           | 245 ± 55                               | 249 ± 58    | 253 ± 48    | 0.26           |
| sVCAM-1, μg/L          |                                    |             |             |                |                                    |             |             |                |  |             |             |                |
| Model I                | 546 ± 134                          | 533 ± 127   | 510 ± 113   | <0.01          | 518 ± 119                          | 527 ± 129   | 540 ± 126   | <0.01          | 532 ± 130                              | 534 ± 124   | 531 ± 119   | 0.68           |
| Model II               | 540 ± 128                          | 532 ± 127   | 514 ± 111   | <0.05          | 524 ± 125                          | 529 ± 127   | 537 ± 125   | <0.05          | 529 ± 132                              | 530 ± 122   | 533 ± 121   | 0.57           |
| Model III              | 531 ± 127                          | 528 ± 126   | 520 ± 110   | <0.05          | 530 ± 122                          | 533 ± 126   | 532 ± 121   | 0.41           | 526 ± 129                              | 531 ± 122   | 534 ± 120   | 0.19           |

<sup>1</sup> Values are geometric means ± sd.

<sup>2</sup> P-values are based on log-transformed values (analysis of covariance).

<sup>3</sup> Model I, Adjusted for age.

<sup>4</sup> Model II, Further adjusted for smoking, physical activity, current estrogen use, menopausal status, family history of diabetes and stroke, and energy intake.

<sup>5</sup> Additionally adjusted for BMI and WC.

markers for inflammatory processes involved in atherosclerosis (33). Investigators from the Nurses' Health Study reported an inverse relation between a prudent dietary pattern and plasma concentrations of CRP and E-selectin, and positive relations between a western dietary pattern and concentrations of CRP, IL-6, E-selectin, sICAM-1, and sVCAM-1 (22). Plasma concentrations of CRP were also positively related to a western dietary pattern in a subgroup of participants in the Health Professional Follow-Up Study (34). Such associations have also recently been reported from the Multi-Ethnic Study of Atherosclerosis (24). Using reduced rank regression for obtaining dietary patterns, Schulze et al. (23) identified a dietary pattern (high in sugar-sweetened soft drinks, refined grains, diet soft drinks, and processed meat but low in wine, coffee, cruciferous vegetables, and yellow vegetables) that was strongly related to inflammatory markers in a nested case-control study, even after control for BMI. Associations of dietary patterns with inflammatory markers were also shown for some priori dietary patterns, such as the Mediterranean dietary pattern; adherence to this traditional dietary pattern in a Greek population was associated with lower concentrations of markers of vascular inflammation (35). Although taken from a very different population, our findings for the healthy and

western patterns were similar to those of earlier studies. Besides epidemiologic studies, an effect of dietary patterns on inflammatory markers was also demonstrated by clinical trials. In a well-designed study by Esposito et al. (16) among patients with the metabolic syndrome, consumption of a Mediterranean-style diet for 2 y improved inflammatory markers and endothelial function more than that did a cardiac-healthy diet (fat intake <30%), even after controlling for weight loss. However, such findings have not been confirmed in patients with coronary artery disease (36); the results may be obscured by pharmacological treatment of these patients.

In line with other epidemiologic studies, we also found that a healthy dietary pattern was associated with lower plasma concentrations of some inflammatory markers (CRP, E-selectin, and sVCAM-1). However, the association with E-selectin levels may be mediated in part by BMI and WC. The major contributing foods to our healthy dietary pattern were fruits and vegetables, which have been shown to be inversely related to markers of inflammation or endothelial function (37,38). Higher content of vitamin C (38) and fiber (39) of these foods may mediate their beneficial effects on the risk markers. However, the inverse relation of the healthy pattern to inflammatory markers

**TABLE 3** Linear regression analysis of the associations between dietary patterns and circulating concentrations of inflammatory markers<sup>1</sup>

|                         | Healthy pattern |        | Western pattern |        | Traditional pattern |       |
|-------------------------|-----------------|--------|-----------------|--------|---------------------|-------|
|                         | $\beta$         | P      | $\beta$         | P      | $\beta$             | P     |
| Unadjusted              |                 |        |                 |        |                     |       |
| Log CRP                 | -0.09           | <0.001 | 0.08            | <0.001 | 0.006               | 0.89  |
| Log TNF- $\alpha$       | -0.03           | 0.12   | 0.003           | 0.51   | -0.009              | 0.85  |
| Log SAA                 | 0.005           | 0.78   | 0.11            | 0.014  | -0.003              | 0.73  |
| Log IL-6                | -0.003          | 0.39   | 0.09            | <0.001 | 0.01                | 0.19  |
| Log E-selectin          | -0.07           | 0.034  | 0.005           | 0.66   | 0.008               | 0.64  |
| Log sICAM-1             | -0.005          | 0.86   | 0.05            | 0.032  | 0.001               | 0.77  |
| Log sVCAM-1             | -0.08           | <0.001 | 0.07            | 0.015  | 0.005               | 0.51  |
| Adjusted for BMI and WC |                 |        |                 |        |                     |       |
| Log CRP                 | -0.05           | 0.011  | 0.02            | 0.095  | 0.004               | 0.93  |
| Log TNF- $\alpha$       | -0.009          | 0.65   | -0.001          | 0.33   | 0.0003              | 0.89  |
| Log SAA                 | 0.006           | 0.43   | 0.06            | 0.039  | 0.001               | 0.81  |
| Log IL-6                | 0.001           | 0.69   | 0.07            | <0.001 | 0.04                | 0.045 |
| Log E-selectin          | -0.02           | 0.13   | -0.0001         | 0.49   | 0.03                | 0.074 |
| Log sICAM-1             | 0.01            | 0.49   | 0.009           | 0.21   | 0.006               | 0.69  |
| Log sVCAM-1             | -0.04           | 0.027  | 0.003           | 0.59   | 0.009               | 0.46  |

<sup>1</sup> All regression models were adjusted for age, physical activity, cigarette smoking, menopausal status, current estrogen replacement therapy, family history of diabetes and stroke, systolic and diastolic blood pressure, plasma levels of total cholesterol, HDL and LDL cholesterol and triglycerides, and energy intake.

may not be confined to its fruit and vegetable content; other foods such as tea (19), fish (40), and whole grains (18) in this pattern may contribute to the associations. With respect to the western dietary pattern, we observed a positive association with CRP, SAA, IL-6, sICAM-1, and sVCAM-1 levels; most of them were accounted for by BMI and WC, except for SAA and IL-6, which were not fully mediated through obesity measures. This finding is not surprising, because the western dietary pattern includes a collection of unhealthy foods such as high-fat dairy, butter, red meat, and other sources of cholesterol and saturated and trans fatty acids, the nutrients well known for their harmful effects on cardiovascular health (17,20,41). Our traditional dietary pattern, characterized by high intake of refined grains and hydrogenated fats, was significantly associated with plasma levels of IL-6 in the full model including BMI and WC. Although the complex nature of this dietary pattern makes interpretation difficult, interaction between foods in this pattern may explain such finding to some extent. High loading factors of refined grains and hydrogenated fats in this dietary pattern is not surprising, because dependence on bread and rice as major energy sources is characteristic of the Iranian diet and hydrogenated cooking fats are the major sources of fat in the Iranian diet, as previous studies showed (42).

Accumulating body fat is associated with insulin resistance, which in turn is the underlying cause of the metabolic syndrome. A large volume of evidence has shown elevated levels of inflammatory markers in obese individuals. Adipose tissue expresses cytokines such as TNF- $\alpha$  and IL-6 (43), which stimulate the production of acute-phase proteins such as CRP by the liver (43). Elevated plasma levels of CRP, TNF- $\alpha$ , and IL-6 are associated with the risk of insulin resistance and atherosclerosis (44). On the other hand, endothelial cells are upregulated in response to inflammatory stimuli and express cellular adhesion molecules (45). Increased levels of these adhesion molecules were reported in diabetic patients and in nondiabetics with insulin

resistance (46). Therefore, it seems that obesity can promote inflammation and endothelial dysfunction and in this way can result in atherosclerosis. In this study, we did not control for obesity measures (BMI and WC) in our main analysis, because these measures may mediate the effect of dietary patterns on inflammatory markers. However, as reflected in our secondary analysis, the associations were not fully mediated by these measures in some cases, suggesting an independent-of-obesity association between diet and cardiovascular disease.

This study has several limitations. First, as we did not consider participants' dietary behaviors in our dietary pattern analysis, one cannot exclude the possibility of residual confounding in the associations we observed. Second, we cannot infer causality because of the cross-sectional design of the study. Third, like any other measurements, dietary assessment also has its own measurement errors. Fourth, limitations of factor analysis that originate from several subjective or arbitrary decisions should also be taken into account (47). Fifth, we cannot generalize about dietary patterns throughout the country, because dietary intakes and other lifestyle measures in Tehran are somewhat different from those in other parts of the country. Moreover, these dietary patterns are confined to women. In addition, inflammatory markers, especially CRP, fluctuate over time and during illnesses (48). This may be problematic for risk stratification and treatment monitoring. So, repeated measurement of these markers could help to discriminate those at high risk. This study also has several strengths. We measured known potential confounding factors and controlled them in our analysis. Furthermore, the uniform background of the study participants in terms of occupation, sex, and education made it unlikely that the results were biased by any unknown confounding factor; however, this uniformity limits the extent to which we may generalize our findings. Another strength of our study was that participants were selected from 4 large socioeconomically diverse districts of Tehran, covering a broad range of dietary habits.

In conclusion, our findings suggest an independent association between major dietary patterns and plasma concentrations of markers of inflammation and lend further support to the notion that the effects of major dietary patterns on risk of chronic diseases might be mediated through their effects on plasma concentrations of inflammatory markers.

## Literature Cited

- Ramos EJ, Xu Y, Romanova I, Middleton F, Chen C, Quinn R, Inui A, Das U, Meguid MM. Is obesity an inflammatory disease? *Surgery*. 2003;134:329-35.
- Williams KJ, Tabas I. Atherosclerosis and inflammation. *Science*. 2002; 297:521-2.
- Dandona P, Aljada A, Chaudhuri A, Mohanty P, Garg R. Metabolic syndrome: a comprehensive perspective based on interactions between obesity, diabetes and inflammation. *Circulation*. 2005;111:1448-54.
- Panagiotakos DB, Pitsavos C, Yannakoulia M, Chrysohoou C, Stefanadis C. The implication of obesity and central fat on markers of chronic inflammation: the ATTICA Study. *Atherosclerosis*. 2005;183: 308-15.
- Theuma P, Fonseca VA. Inflammation and emerging risk factors in diabetes mellitus and atherosclerosis. *Curr Diab Rep*. 2003;3: 248-54.
- Haffner SM. The metabolic syndrome: inflammation, diabetes mellitus, and cardiovascular disease. *Am J Cardiol*. 2006;97:3-11.
- Takeuchi N, Kawamura T, Kanai A, Nakamura N, Uno T, Hara T, Sano T, Sakamoto N, Hamada Y, et al. The effect of cigarette smoking on soluble adhesion molecules in middle-aged patients with Type 2 diabetes mellitus. *Diabet Med*. 2002;19:57-64.

8. DeSouza CA, Dengel DR, Macko RF, Cox K, Seals DR. Elevated levels of circulating cell adhesion molecules in uncomplicated essential hypertension. *Am J Hypertens*. 1997;10:1335-41.
9. Calabresi L, Gomarasci M, Villa B, Omoboni L, Dmitrieff C, Franceschini G. Elevated soluble cellular adhesion molecules in subjects with low HDL-cholesterol. *Arterioscler Thromb Vasc Biol*. 2002;22:656-61.
10. Hackman A, Abe Y, Insull W Jr, Pownall H, Smith L, Dunn K, Gotto AM Jr, Ballantyne CM. Levels of soluble cell adhesion molecules in patients with dyslipidemia. *Circulation*. 1996;93:1334-8.
11. Barinas-Mitchell E, Cushman M, Meilahn EN, Tracy RP, Kuller LH. Serum levels of C-reactive protein are associated with obesity, weight gain, and hormone replacement therapy in healthy postmenopausal women. *Am J Epidemiol*. 2001;153:1094-101.
12. Tracy RP, Psaty BM, Macy E, Bovill EG, Cushman M, Cornell ES, Kuller LH. Lifetime smoking exposure affects the association of C-reactive protein with cardiovascular disease risk factors and subclinical disease in healthy elderly subjects. *Arterioscler Thromb Vasc Biol*. 1997;17:2167-76.
13. Laimer M, Ebenbichler CF, Kaser S, Sandhofer A, Weiss H, Nehoda H, Aigner F, Patsch JR. Markers of chronic inflammation and obesity: a prospective study on the reversibility of this association in middle-aged women undergoing weight loss by surgical intervention. *Int J Obes Relat Metab Disord*. 2002;26:659-62.
14. Tchernof A, Nolan A, Sites CK, Ades PA, Poehlman ET. Weight loss reduces C-reactive protein levels in obese postmenopausal women. *Circulation*. 2002;105:564-9.
15. Fung TT, McCullough ML, Newby PK, Manson JE, Meigs JB, Rifai N, Willett WC, Hu FB. Diet-quality scores and plasma concentrations of markers of inflammation and endothelial dysfunction. *Am J Clin Nutr*. 2005;82:163-73.
16. Esposito K, Marfella R, Ciotola M, Di Palo C, Giugliano F, Giugliano G, D'Armiendo M, D'Andrea F, Giugliano D. Effect of a Mediterranean-style diet on endothelial dysfunction and markers of vascular inflammation in the metabolic syndrome: a randomized trial. *JAMA*. 2004;292:1440-6.
17. Lopez-Garcia E, Schulze MB, Meigs JB, Manson JE, Rifai N, Stampfer MJ, Willett WC, Hu FB. Consumption of trans fatty acids is related to plasma biomarkers of inflammation and endothelial dysfunction. *J Nutr*. 2005;135:562-6.
18. Qi L, van Dam RM, Liu S, Franz M, Mantzoros C, Hu FB. Whole-grain, bran, and cereal fiber intakes and markers of systemic inflammation in diabetic women. *Diabetes Care*. 2006;29:207-11.
19. De Bacquer D, Clays E, Delanghe J, De Backer G. Epidemiological evidence for an association between habitual tea consumption and markers of chronic inflammation. *Atherosclerosis*. 2006;189:428-35. Epub 2006 Jan 25.
20. Mozaffarian D, Pischon T, Hankinson SE, Rifai N, Joshipura K, Willett WC, Rimm EB. Dietary intake of trans fatty acids and systemic inflammation in women. *Am J Clin Nutr*. 2004;79:606-12.
21. Pischon T, Hankinson SE, Hotamisligil GS, Rifai N, Willett WC, Rimm EB. Habitual dietary intake of n-3 and n-6 fatty acids in relation to inflammatory markers among US men and women. *Circulation*. 2003;108:155-60.
22. Lopez-Garcia E, Schulze MB, Fung TT, Meigs JB, Rifai N, Manson JE, Hu FB. Major dietary patterns are related to plasma concentrations of markers of inflammation and endothelial dysfunction. *Am J Clin Nutr*. 2004;80:1029-35.
23. Schulze MB, Hoffmann K, Manson JE, Willett WC, Meigs JB, Weikert C, Heidemann C, Colditz GA, Hu FB. Dietary pattern, inflammation, and incidence of type 2 diabetes in women. *Am J Clin Nutr*. 2005;82:675-84.
24. Nettleton JA, Steffen LM, Mayer-Davis EJ, Jenny NS, Jiang R, Herrington DM, Jacobs DR Jr. Dietary patterns are associated with biochemical markers of inflammation and endothelial activation in the Multi-Ethnic Study of Atherosclerosis (MESA). *Am J Clin Nutr*. 2006;83:1369-79.
25. Hu FB. Dietary pattern analysis: a new direction in nutritional epidemiology. *Curr Opin Lipidol*. 2002;13:3-9.
26. Ghaffarpour M, Houshiar-Rad A, Kianfar H. The manual for household measures, cooking yields factors and edible portion of foods. Tehran: Keshaverzi Press; 1999. p. 1-46. (in Farsi)
27. Sarkissian N, Azar M. Food composition table of Iran. 1st ed. Islamic Republic of Iran, Institute of Nutrition Sciences and Food Technology; 1980, Report No.: 131.
28. National Nutrient Database for Standard Reference Release 17 [database on the Internet]. Washington: USDA. [cited 2005 Sep 19]. Available from: <http://www.nal.usda.gov/fnic/foodcomp>.
29. Esmailzadeh A, Mirmiran P, Azizi F. Whole-grain intake and the prevalence of the hypertriglyceridemic waist phenotype in Tehranian adults. *Am J Clin Nutr*. 2005;81:55-63.
30. Esmailzadeh A, Mirmiran P, Azizi F. Whole-grain consumption and the metabolic syndrome: a favorable association in Tehranian adults. *Eur J Clin Nutr*. 2005;59:353-62.
31. Ainsworth BE, Haskell WL, Whitt MC, Irwin ML, Swartz AM, Strath SJ, O'Brien WL, Bassett DR Jr, Schmitz KH, et al. Compendium of physical activities: an update of activity codes and MET intensities. *Med Sci Sports Exerc*. 2000;32:S498-504.
32. Kim J-O, Mueller CW. Factor analysis: statistical methods and practical issues. Thousand Oaks (CA): Sage Publications; 1978.
33. Lucas AR, Korol R, Pepine CJ. Inflammation in atherosclerosis: some thoughts about acute coronary syndromes. *Circulation*. 2006;113:e728-32.
34. Fung TT, Rimm EB, Spiegelman D, Rifai N, Tofler GH, Willett WC, Hu FB. Association between dietary patterns and plasma biomarkers of obesity and cardiovascular disease risk. *Am J Clin Nutr*. 2001;73:61-7.
35. Chrysohoou C, Panagiotakos DB, Pitsavos C, Das UN, Stefanadis C. Adherence to the Mediterranean diet attenuates inflammation and coagulation process in healthy adults: the ATTICA Study. *J Am Coll Cardiol*. 2004;44:152-8.
36. Michalsen A, Lehmann N, Pithan C, Knoblauch NT, Moebus S, Kannenberg F, Binder L, Budde T, Dobos GJ. Mediterranean diet has no effect on markers of inflammation and metabolic risk factors in patients with coronary artery disease. *Eur J Clin Nutr*. 2006;60:478-85.
37. Lowe GDO, Woodward M, Rumley A, Morrison C, Tunstall-Pedoe H, Stephen K. Total tooth loss and prevalent cardiovascular disease in men and women: possible roles of citrus fruit consumption, vitamin C, and inflammatory and thrombotic variables. *J Clin Epidemiol*. 2003;56:694-700.
38. Wannamethee SG, Lowe GD, Rumley A, Bruckdorfer KR, Whincup PH. Associations of vitamin C status, fruit and vegetable intakes, and markers of inflammation and hemostasis. *Am J Clin Nutr*. 2006;83:567-74.
39. Ma Y, Griffith JA, Chasan-Taber L, Olenzki BC, Jackson E, Stanek EJ, Li W, Pagoto SL, Hafner AR, et al. Association between dietary fiber and serum C-reactive protein. *Am J Clin Nutr*. 2006;83:760-6.
40. Zampelas A, Panagiotakos DB, Pitsavos C, Das UN, Chrysohoou C, Skoumas Y, Stefanadis C. Fish consumption among healthy adults is associated with decreased levels of inflammatory markers related to cardiovascular disease: the ATTICA Study. *J Am Coll Cardiol*. 2005;46:120-4.
41. Han SN, Leka LS, Lichtenstein AH, Ausman LM, Schaefer EJ, Meydani SN. Effect of hydrogenated and saturated, relative to polyunsaturated, fat on immune and inflammatory responses of adults with moderate hypercholesterolemia. *J Lipid Res*. 2002;43:445-52.
42. Kimiagar SM, Ghaffarpour M, Houshiar-Rad A, Hormozdaryi H, Zellipour L. Food consumption pattern in the Islamic Republic of Iran and its relation to coronary heart disease. *East Mediterr Health J*. 1998;4:539-47.
43. Yudkin JS, Stehouwer CD, Emeis JJ, Coppack SW. C-reactive protein in healthy subjects: associations with obesity, insulin resistance, and endothelial dysfunction: a potential role for cytokines originating from adipose tissue? *Arterioscler Thromb Vasc Biol*. 1999;19:972-8.
44. Yudkin JS, Kumari M, Humphries SE, Mohamed-Ali V. Inflammation, obesity, stress and coronary heart disease: is interleukin-6 the link? *Atherosclerosis*. 2000;148:209-14.
45. Gearing AJ, Newman W. Circulating adhesion molecules in disease. *Immunol Today*. 1993;14:506-12.
46. Blankenberg S, Barbaux S, Tiret L. Adhesion molecules and atherosclerosis. *Atherosclerosis*. 2003;170:191-203.
47. Martinez ME, Marshall JR, Sechrest L. Invited commentary: factor analysis and the search for objectivity. *Am J Epidemiol*. 1998;148:17-21.
48. Bogaty P, Brophy JM, Boyer L, Simard S, Joseph L, Bertrand F, Dagenais GR. Fluctuating inflammatory markers in patients with stable ischemic heart disease. *Arch Intern Med*. 2005;165:221-6.

## APPENDIX

### Appendix 1. Food grouping used in the dietary pattern analyses

| Food groups             | Food items   |
|-------------------------|--|
| Processed meats         | Sausages   |
| Red meats               | Beef, hamburger, lamb  |
| Organ meats             | Beef liver   |
| Fish                    | Canned tuna fish, other fish   |
| Poultry                 | Chicken with or without skin   |
| Eggs                    | Eggs   |
| Butter                  | Butter   |
| Margarine               | Margarine  |
| Low-fat dairy products  | Skim or low-fat milk, low-fat yoghurt  |
| High-fat dairy products | High-fat milk, whole milk, chocolate milk, cream, high-fat yoghurt, cream yoghurt, cream cheese, other cheeses, ice cream  |
| Tea                     | Tea  |
| Coffee                  | Coffee   |
| Fruits                  | Pears, apricots, cherries, apples, raisins or grapes, bananas, cantaloupe, watermelon, oranges, grapefruit, kiwi, grapefruits, strawberries, peaches, nectarines, tangerines, mulberries, plums, persimmons, pomegranates, lemons, pineapples, fresh figs, dates |
| Fruit juices            | Apple juice, orange juice, grapefruit juice, other fruit juices  |
| Cruciferous vegetables  | Cabbage, cauliflower, Brussels sprouts, kale   |
| Yellow vegetables       | Carrots  |
| Tomatoes                | Tomatoes, tomato sauce, tomato pasta   |
| Green leafy vegetables  | Spinach, lettuce   |
| Other vegetables        | Cucumbers, mixed vegetables, eggplant, celery, green peas, green beans, green peppers, turnips, corn, squash, mushrooms, onions  |
| Legumes                 | Beans, peas, lima beans, broad beans, lentils, soy   |
| Garlic                  | Garlic   |
| Potatoes                | Potatoes   |
| French fries            | French fries   |
| Whole grains            | Dark breads (Sangak, Barbari, Taftoon), barley bread, popcorn, cornflakes, wheat germ, bulgur  |
| Refined grains          | White breads (Lavash, baguette), noodles, pasta, rice, toasted bread, milled barley, sweet bread, white flour, starch, biscuits  |
| Pizza                   | Pizza  |
| Snacks                  | Potato chips, puffs, crackers, popcorn   |
| Nuts                    | Peanuts, almonds, pistachios, hazelnuts, roasted seeds, walnuts  |
| Mayonnaise              | Mayonnaise   |
| Dried fruits            | Dried figs, dried dates, dried mulberries, other dried fruits  |
| Olive                   | Olives, olive oils   |
| Sweets and desserts     | Chocolates, cookies, cakes, confections  |
| Hydrogenated fats       | Hydrogenated fats, animal fats   |
| Vegetable oils          | Vegetable oils (except for olive oil)  |
| Sugars                  | Sugars, candies, tamarisk (kind of confectionery)  |
| Condiments              | Jam, jelly, honey  |
| Soft drinks             | Soft drinks  |
| Dough                   | Dough  |
| Broth                   | Broth  |
| Salt                    | Salt   |
| Pickles                 | Pickles  |

### Appendix 2. Factor-loading matrix for major dietary patterns<sup>1</sup>

| Food groups             | Dietary patterns |         |             |
|-------------------------|------------------|---------|-------------|
|                         | Healthy          | Western | Traditional |
| Fruits                  | 0.74             | -0.29   | —           |
| Other vegetables        | 0.71             | -0.31   | —           |
| Tomatoes                | 0.63             | —       | —           |
| Poultry                 | 0.53             | —       | —           |
| Legumes                 | 0.52             | —       | 0.26        |
| Cruciferous vegetables  | 0.47             | —       | —           |
| Green leafy vegetables  | 0.41             | —       | —           |
| Tea                     | 0.39             | —       | 0.42        |
| Fruit juices            | 0.37             | 0.21    | —           |
| Whole grains            | 0.34             | —       | 0.40        |
| Butter                  | -0.31            | 0.43    | —           |
| Potatoes                | 0.29             | 0.35    | 0.46        |
| Low-fat dairy products  | 0.26             | -0.37   | —           |
| High-fat dairy products | -0.23            | 0.39    | —           |
| Fish                    | 0.22             | -0.29   | —           |
| Yellow vegetables       | 0.21             | —       | —           |
| Hydrogenated fats       | -0.20            | 0.34    | 0.28        |
| Refined grains          | —                | 0.66    | 0.51        |
| Red meats               | —                | 0.56    | —           |
| Processed meats         | —                | 0.39    | —           |
| Sweets and desserts     | —                | 0.37    | —           |
| Pizza                   | —                | 0.36    | —           |
| Eggs                    | —                | 0.35    | —           |
| Soft drinks             | —                | 0.33    | —           |
| Snacks                  | —                | 0.29    | —           |
| French fries            | —                | 0.24    | —           |
| Coffee                  | —                | 0.23    | —           |
| Mayonnaise              | —                | 0.22    | —           |
| Casserole               | —                | —       | 0.23        |
| Nuts                    | —                | —       | —           |
| Olive                   | —                | —       | —           |
| Sugars                  | —                | —       | —           |
| Condiments              | —                | —       | —           |
| Vegetable oils          | —                | 0.20    | —           |
| Dough                   | —                | —       | —           |
| Organ meats             | —                | —       | —           |
| Margarine               | —                | —       | —           |
| Dried fruits            | —                | —       | —           |
| Salt                    | —                | —       | —           |
| Garlic                  | —                | —       | —           |
| Pickles                 | —                | —       | —           |
| Variance explained, %   | 0.103            | 0.086   | 0.052       |

<sup>1</sup> Values <0.20 were excluded for simplicity.