Fruit and vegetable intakes, C-reactive protein, and the metabolic syndrome[1–3]

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ABSTRACT

Background: Limited data on the relation between the risk of the metabolic syndrome and fruit and vegetable intakes and inflammatory marker concentrations are available.

Objective: We evaluated the relation between fruit and vegetable intakes and C-reactive protein (CRP) concentrations and the prevalence of the metabolic syndrome.

Design: Fruit and vegetable intakes were assessed with the use of a validated semiquantitative food-frequency questionnaire in a cross-sectional study of 486 Tehrani female teachers aged 40–60 y. Anthropometric measurements were made and blood pressure was assessed according to standard methods. Fasting blood samples were taken for biochemical measurements. The metabolic syndrome was defined on the basis of the National Cholesterol Education Program Adult Treatment Panel III guidelines.

Results: The reported mean daily fruit and vegetable intakes were 228 ± 79 and 186 ± 88 g/d, respectively. Both fruit and vegetable intakes were inversely associated with plasma CRP concentrations. After statistical control for age, body mass index, and waist circumference, mean plasma CRP concentrations across increasing quintile categories of fruit intakes were 1.94, 1.79, 1.65, 1.61, and 1.56 mg/L and of vegetable intakes were 2.03, 1.82, 1.58, 1.52, and 1.47 mg/L (P for trend < 0.01 for both). These inverse associations remained significant after additional control for other potential confounding variables and dietary factors. After control for potential confounders, persons in the highest quintile of fruit intake had a 34% (95% CI: 20%, 46%) lower and those in the highest quintile of vegetables intake had a 30% (95% CI: 16%, 39%) lower chance of having the metabolic syndrome than did those in the lowest quintiles.

Conclusions: Higher intakes of fruit and vegetables are associated with a lower risk of the metabolic syndrome; the lower risk may be the result of lower CRP concentrations. These findings support current dietary recommendations to increase daily intakes of fruit and vegetables as a primary preventive measure against cardiovascular disease. *Am J Clin Nutr* 2006;84:1489–97.

KEY WORDS Fruit intake, vegetable intake, metabolic syndrome, cardiovascular disease risk factors, inflammation

INTRODUCTION

The term *metabolic syndrome*, since the work of Reaven (1), refers to the state in which metabolic risk factors are clustered in persons. This syndrome is emerging as one of the major medical and public health problems in the United States (2) and worldwide (3–5), and persons with this syndrome have an increased risk of morbidity and mortality due to cardiovascular disease and diabetes (6, 7). In Tehran, Iran, >30% of adults (8) and 10% of adolescents (9) are affected. The dietary determinants of this syndrome remain to be identified (10–12).

Although many studies have investigated the role of fruit and vegetable intakes in chronic diseases (13–17), data directly relating intakes of fruit and vegetables to the risk of the metabolic syndrome are scant. Intakes of fruit and vegetables may reduce the risk of the metabolic syndrome through the beneficial combination of antioxidants, fiber, potassium, magnesium, and other phytochemicals. Fruit and vegetables have been shown to be associated with a reduced risk of coronary heart disease (18–20), but the mechanisms have not been well understood. Systemic inflammation, as evidenced by plasma C-reactive protein (CRP) concentrations, has been frequently suggested as a possible mechanism through which diet can affect the development of chronic diseases (21–23). As recently reported, CRP may directly affect cardiovascular disease through a complement-mediated process (24). Fruit and vegetable consumption may reduce the risk of coronary heart disease in part through the lowering of CRP concentrations. However, limited data exist regarding the association of fruit and vegetable intakes with CRP (25, 26). This study was, therefore, undertaken to assess the association of fruit and vegetable intakes with blood CRP concentrations and the prevalence of the metabolic syndrome among female teachers aged 40–60 y living in Tehran.

SUBJECTS AND METHODS

Subjects

This cross-sectional study was conducted among a representative sample of female teachers aged 40–60 y living in Tehran

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selected by a multistage cluster random sampling method. A random sample of 583 female teachers were invited to participate in the current study, and 521 women agreed to do so. Participants with a history of cardiovascular disease, diabetes, cancer, or stroke were excluded because of possible changes in diet associated with these conditions. We also excluded subjects who had left >70 items blank on the food-frequency questionnaire (FFQ), who reported a total daily energy intake outside the range of 800–4200 kcal, and who were taking medications that would affect serum lipoprotein, blood pressure, and carbohydrate metabolism. These exclusions resulted in 486 subjects for the present analysis. This study was approved by the research council of National Nutrition and Food Technology Research Institute, Shaheed Beheshti University of Medical Sciences, and written informed consent was obtained from each participant.

Assessment of dietary intake

Usual dietary intake was assessed with the use of a validated 168-item semiquantitative FFQ. All the FFQs were administered by a trained dietitian. 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 (eg, bread), weekly (eg, rice and meat), or monthly (eg, fish) basis. The reported frequency of consumption for each food item was then converted to a daily intake. Portion sizes of consumed foods were converted to grams by using household measures (27). Total energy intake was calculated by summing up energy intakes from all foods.

We considered fruit to be pears, apricots, cherries, apples, raisins or grapes, bananas, cantaloupe, watermelon, oranges, grapefruit, kiwi, strawberries, peaches, nectarines, tangerines, mulberry, plums, persimmons, pomegranates, lemons, pineapples, fresh figs, and dates. In the vegetable food group, we included cabbage, cauliflower, Brussels sprouts, kale, carrots, tomatoes, spinach, lettuce, cucumber, mixed vegetables, eggplant, celery, green peas, green beans, green pepper, turnip, corn, squash, mushrooms, and onions.

The reliability of the FFQ was evaluated in a randomly chosen 132 participants (not included in this study) by comparing nutrient consumption determined using responses to the FFQ on 2 occasions 1 y apart (11, 12). The correlation coefficients for the repeatability of FFQ for fruit and vegetables were 0.71 and 0.74, respectively. The FFQ also had high reliability for nutrients. For example, the correlation coefficients were 0.81 for dietary fiber and 0.85 for magnesium. Comparative validity was determined by comparison with intakes estimated from the average of twelve 24-h dietary recalls (one for each month of the year). Preliminary analysis of the validation study showed that nutrients commonly found in fruit and vegetables were moderately correlated between these 2 methods after total energy intake was controlled for. These correlation coefficients were 0.69 for dietary fiber and 0.67 for magnesium intake. The validity of the FFQ for assessing fruit and vegetable intakes was also good; the correlation coefficients for a comparison between the FFQ and detailed dietary recalls were 0.61 for fruit and 0.57 for vegetables. Overall, these data indicate that the FFQ provides reasonably valid measures of average long-term dietary intakes.

Assessment of anthropometric measures

Weight was measured to the nearest 100 g with digital scales while the subjects were minimally clothed and not wearing shoes. Height was measured while the subjects were standing and not wearing shoes by using a tape measure while the shoulders were in a normal position. Body mass index (BMI) was calculated and expressed in kg/m^2. Waist circumference was measured at the narrowest level and that of the hip at the maximum level over light clothing with the use of an unstretched tape measure and no pressure to the body surface; measurements were recorded to the nearest 0.1 cm. As the measurements were made, the participants were asked to remove belts and tight or loose garments intended to alter the shape of the body; the person doing the measuring was asked to ensure that the tape had the proper tension, neither too loose nor too tight. Although the narrowest point of the waist is easy to identify in most people, it was not evident in some of the participants because of either a large amount of abdominal fat or extreme thinness (28). In the current study, when the narrowest point of waist was difficult to identify (particularly in obese persons), we measured waist circumference immediately below the end of the lowest rib, because, in most persons, the narrowest point of the waist is at the lowest rib (28). To reduce subjective error, all measurements were taken by the same technician.

Assessment of biomarkers

A blood sample was drawn between 0700 and 0900 into evacuated tubes from all study participants after they fasted overnight for 12 h. Blood samples were taken while the subjects were in a sitting position, according to a standard protocol, and centrifuged within 30–45 min of collection. The analysis of samples was performed by using Selectra-2 auto-analyzer (Vital Scientific, Spankeren, Netherlands). Fasting plasma glucose was measured on the day of blood collection with an enzymatic colorimetric method using glucose oxidase. Serum triacylglycerol concentrations were assayed with the use of triacylglycerol kits (Pars Azmoon Inc, Tehran, Iran) by enzymatic colorimetric tests with glycerol phosphate oxidase. HDL cholesterol was measured after precipitation of the apolipoprotein B–containing lipoproteins with phosphotungstic acid. CRP concentrations were measured by using an ultrasensitive latex-enhanced immunoturbidimetric assay (Randox laboratory Ltd, Belfast, United Kingdom). The inter- and intraassay CVs for CRP were 4.8% and 7.6%, respectively.

Assessment of blood pressure

For the measurement of blood pressure, the participants initially rested for 15 min. A qualified person then measured blood pressure 3 times with a standard mercury sphygmomanometer while the subjects were in a seated position; the mean of the 3 measurements was considered to be the participant's blood pressure. The systolic blood pressure was defined as the appearance of the first sound (Korotkoff phase 1), and the diastolic blood pressure was defined as the disappearance of the sound (Korotkoff phase 5) during deflation of the cuff at a 2–3 mm per second decrement rate of the mercury column.

Assessment of other variables

Data on physical activity were obtained by administering a pretested oral questionnaire to the participants; physical activity was expressed as metabolic equivalent hours per week (MET-h/

wk) (29). Additional covariate information regarding age, smoking habits, menopausal status, medical history, and current use of medications was obtained by using questionnaires.

Definition of terms

Obesity was defined as a BMI ≥ 30 (30). Metabolic syndrome was defined as the presence of ≥3 of the following components as recommended by the National Cholesterol Education Program Adult Treatment Panel III (ATP III) (31): *1*) abdominal adiposity (waist circumference > 88 cm), *2*) low serum HDL cholesterol (<50 mg/dL), *3*) high serum triacylglycerol (≥150 mg/dL), *4*) elevated blood pressure [≥130 (systolic)/85 (diastolic) mm Hg], and *5*) abnormal glucose homeostasis (fasting plasma glucose ≥ 110 mg/dL).

Statistical methods

The Statistical Package for Social Science (version 9.05; SPSS Inc, Chicago IL) was used for all statistical analyses. The participants were categorized according to quintiles of fruit and vegetable intakes. Significant differences in general characteristics across quintile categories of fruit and vegetable intakes were evaluated by using one-way analysis of variance with Tukey's post hoc comparisons. Chi-square tests were used to detect any significant differences in the distribution of subjects across quintile categories with regard to qualitative variables. We determined age- and energy-adjusted means for dietary variables across quintiles of fruit and vegetable intakes by using a general linear model (GLM). Analysis of covariance with Bonferroni correction was used to compare these means. Mean plasma concentrations of CRP were computed across quintiles of fruit and vegetable intakes in different models. First, we adjusted for age (continuous), BMI (continuous), and waist circumference (continuous). In the second model we additionally adjusted for smoking (yes or no), physical activity (continuous), total energy intake (continuous), use of estrogen (yes or no), menopausal status (yes or no), and family history of diabetes or stroke (yes or no). Finally, we added dietary variables into the model, including percentage of energy from fat, the mutual effects of fruit or vegetables (all as continuous variables), and intakes of cholesterol, meat and fish, dairy products, and whole and refined grains. Analysis of covariance was used for comparison of mean CRP concentrations across quintiles. To determine the association of fruit and vegetable intakes with the metabolic syndrome and its features, we used multivariable logistic regression models controlled for age (y), energy intake (kcal/d), cholesterol intake, percentage of energy from fat, cigarette smoking (yes or no), physical activity (in MET-h/wk), current estrogen use (yes or no), menopausal status (yes or no), and family history of diabetes or stroke (yes or no). For dependent variables with which a significant association with fruit and vegetable intakes was observed, we further examined whether dietary patterns associated with high fruit and vegetable intakes would explain these associations by adjusting for intakes of whole grains, refined grains, dairy, and meat and fish. In the third model, we added CRP to the mentioned covariates in the model. We controlled for BMI in the last model to determine whether the associations were mediated by obesity. The odds ratios estimated from logistic regression models in cross-sectional studies are not valid estimators of the rate ratios when the binary outcome variable has a high prevalence (32, 33). Therefore, we used the formula suggested by Zhang and Yu (34) to correct the adjusted odds ratios obtained from logistic regression to derive an estimate of association that better represents the true relative risk. In all multivariate models, the first quintile of fruit and vegetables intake was considered as a reference. The Mantel-Haenszel extension test was performed to assess the overall trend of odds ratios across increasing quintiles of fruit and vegetables intake.

RESULTS

The reported mean daily intakes of fruit and vegetables were 228 ± 79 and 186 ± 88 g/d, respectively. The food items that

TABLE 1
Characteristics of the study participants by quintiles of fruit and vegetable intakes[1]

	Fruit quintiles				Vegetable quintiles			
	1 (lowest) (n = 98)	3 (n = 97)	5 (highest) (n = 97)	P^2	1 (lowest) (n = 98)	3 (n = 97)	5 (highest) (n = 97)	P^2
Age (y)	51 ± 6[3]	50 ± 6	48 ± 7	< 0.05	49 ± 8	51 ± 7	50 ± 7	0.09
BMI (kg/m^2)	29.9 ± 3.6	27.7 ± 3.9	24.8 ± 4.1	< 0.01	28.9 ± 4.1	26.7 ± 3.4	24.9 ± 3.8	< 0.01
WHR	0.92 ± 0.08	0.88 ± 0.08	0.83 ± 0.08	< 0.01	0.89 ± 0.07	0.86 ± 0.09	0.83 ± 0.08	< 0.01
Waist girth (cm)	98 ± 10	92 ± 11	86 ± 11	< 0.01	97 ± 12	94 ± 11	88 ± 12	< 0.01
Physical activity (MET-h/wk)	12.5 ± 10.1	14.8 ± 10.7	16.6 ± 11.6	< 0.01	12.7 ± 11.8	15.2 ± 10.5	17.1 ± 12.5	< 0.01
Family history of diabetes (%)	11	8	10	< 0.05	9	9	7	< 0.05
Family history of stroke (%)	2	1	1	0.31	1	1	1	0.88
Current daily smokers (%)	1	0	1	0.22	0	1	1	0.15
Obese (%)[4]	43	35	23	< 0.05	37	29	21	< 0.05
Current estrogen use (%)	27	26	25	0.18	25	25	25	0.29
Metabolic syndrome (%)[5]	38	28	19	< 0.05	36	28	17	< 0.05

[1] WHR, waist-to-hip ratio; MET, metabolic equivalent.
[2] ANOVA for quantitative variables and chi-square test for qualitative variables.
[3] $\bar{x}$ ± SD (all such values).
[4] BMI ≥ 30.
[5] Defined as the presence of ≥3 of the following components: *1*) abdominal adiposity (waist circumference > 88 cm), *2*) low serum HDL cholesterol (<50 mg/dL), *3*) high serum triacylglycerol (≥150 mg/dL), *4*) elevated blood pressure [≥130 (systolic)/85 (diastolic) mm Hg], and *5*) abnormal glucose homeostasis (fasting plasma glucose ≥110 mg/dL).

TABLE 2
Dietary intakes of participants by quintiles of fruit and vegetable intakes[1]

	Fruit quintiles				Vegetable quintiles			
Dietary intake	1 (lowest) (n = 98)	3 (n = 97)	5 (highest) (n = 97)	P^2	1 (lowest) (n = 98)	3 (n = 97)	5 (highest) (n = 97)	P^2
Nutrients								
Total energy (kcal/d)	2741 ± 23[3]	2436 ± 25	2381 ± 20	< 0.05	2582 ± 22	2440 ± 27	2331 ± 19	< 0.05
Carbohydrate (% of total energy)	59 ± 1	60 ± 1	58 ± 1	0.09	58 ± 1	59 ± 1	60 ± 1	0.11
Protein (% of total energy)	13.0 ± 0.4	12.0 ± 0.3	12.0 ± 0.4	0.17	12.0 ± 0.3	11.0 ± 0.4	11.0 ± 0.4	0.26
Fat (% of total energy)	28.0 ± 0.7	28.0 ± 0.9	30.0 ± 0.6	0.07	29.0 ± 0.6	30.0 ± 0.8	29.0 ± 0.7	0.13
Cholesterol (mg/d)	209 ± 8	184 ± 11	151 ± 9	< 0.05	241 ± 9	196 ± 10	173 ± 8	< 0.05
Dietary fiber (g/d)	9 ± 1	16 ± 1	24 ± 1	< 0.01	11 ± 1	18 ± 1	27 ± 1	< 0.01
Vitamin B-6 (mg/d)	0.7 ± 0.1	0.9 ± 0.08	1.1 ± 0.1	< 0.05	0.5 ± 0.06	0.8 ± 0.1	1.3 ± 0.09	< 0.05
Magnesium (mg/d)	104 ± 2	137 ± 3	169 ± 2	< 0.05	98 ± 2	138 ± 2	177 ± 3	< 0.01
Foods (g/d)								
Fruit[4]	98 ± 7	217 ± 8	362 ± 6	< 0.01	142 ± 7	259 ± 7	307 ± 9	< 0.01
Vegetables[5]	121 ± 4	217 ± 5	231 ± 7	< 0.05	74 ± 6	191 ± 4	279 ± 7	< 0.01
Meat and fish[6]	111 ± 3	99 ± 2	73 ± 3	< 0.05	123 ± 3	94 ± 3	80 ± 4	< 0.05
Whole grains[7]	41 ± 2	118 ± 3	192 ± 2	< 0.01	64 ± 4	105 ± 2	174 ± 3	< 0.05
Refined grains[8]	283 ± 5	198 ± 6	153 ± 3	< 0.05	262 ± 5	203 ± 5	146 ± 4	< 0.05
Dairy products[9]	176 ± 3	193 ± 4	181 ± 3	0.09	217 ± 4	195 ± 5	184 ± 2	< 0.05

[1] Nutrients and food intakes were adjusted for age and total energy intake.
[2] ANCOVA.
[3] $\bar{x}$ ± SEM (all such values).
[4] Includes pears, apricots, cherries, apples, raisins or grapes, bananas, cantaloupe, watermelon, oranges, grapefruit, kiwi, strawberries, peaches, nectarines, tangerines, mulberries, plums, persimmons, pomegranates, lemons, pineapples, fresh figs, and dates.
[5] Includes cabbage, cauliflower, Brussels sprouts, kale, carrots, tomatoes, spinach, lettuce, cucumber, mixed vegetables, eggplant, celery, green peas, green beans, green pepper, turnip, corn, squash, mushrooms, and onions.
[6] Includes sausages, beef, hamburger, liver, canned tuna fish, other fish, and chicken.
[7] Includes whole-grain breads, barley bread, popcorn, cornflakes, wheat germ, and bulgur.
[8] Includes white breads, noodles, pasta, rice, toasted bread, milled barley, sweet bread, white flour, starch, and biscuits.
[9] Includes milk, cheese, chocolate milk, cream, yogurt, cream cheese, and ice cream.

contributed most to fruit intakes were apples, cantaloupe, watermelon, grapes, and bananas, respectively, and those that contributed most to vegetable intake were onions, tomatoes, mixed vegetables, lettuce, cucumber, and green beans, respectively.

Characteristics of the study participants across quintile categories of fruit and vegetable intakes are shown in **Table 1**. Compared with participants in the lowest quintile, those in the highest quintile of fruit intake were slightly younger, more physically active, and less likely to be obese and had lower anthropometric measures and a lower prevalence of the metabolic syndrome. Similarly, those in the highest category of vegetable intake had lower anthropometric measures and a lower prevalence of obesity and the metabolic syndrome and were more physically active than were those in the lowest category. No significant difference in the distribution of smokers and in current estrogen users across quintile categories of fruit and vegetable intake was observed.

Age- and energy-adjusted means for dietary variables across quintile categories of fruit and vegetable intakes are presented in **Table 2**. Higher intakes of fruit and vegetables were associated with a healthier diet; those subjects in the upper category also consumed less cholesterol, meat, and refined grains and more dietary fiber and whole grains.

Mean plasma CRP concentrations across quintile categories of fruit and vegetable intakes are provided in **Table 3**. Both fruit and vegetable intakes were inversely associated with plasma CRP concentrations. After the statistical control for age, BMI, and waist circumference, mean plasma CRP concentrations across increasing quintile categories of fruit were 1.94, 1.79, 1.65, 1.61, and 1.56 mg/L (P for trend < 0.01) and of vegetables were 2.03, 1.82, 1.58, 1.52, and 1.47 mg/L (P for trend < 0.01). This inverse association remained significant even after additional control for other potential confounding variables and dietary factors. When we considered fruit and vegetable intakes together, this association was more evident even after adjustments were made for potential confounding variables and dietary factors (data not shown).

Compared with those in the lowest quintile of fruit and vegetable intakes, subjects in the highest category had lower odds of having the metabolic syndrome, even after CRP concentrations and lifestyle and dietary confounders were controlled for (**Table 4**). After potential confounders were controlled for, subjects in the highest quintile of fruit intake had a 34% lower and those in the highest quintile of vegetable intake had a 30% lower chance of having the metabolic syndrome. When we considered fruit and vegetable intakes together, the protective effect became even stronger; those in the highest quintile had a 39% lower risk (data not shown). However, all associations became much weaker when we took the BMI into account (Table 4). The same results were obtained when we used International Diabetes Federation criteria for the metabolic syndrome (not shown).

After adjustment for potential confounding variables including dietary factors and CRP, a significant inverse trend was observed between fruit intake and the probability of having the metabolic syndrome features (**Figure 1**). However, no significant

TABLE 3
Plasma C-reactive protein (CRP) concentrations by quintiles of fruit and vegetable intakes[1]

	Fruit quintiles				Vegetable quintiles			
Plasma CRP	1 (lowest) (n = 98)	3 (n = 97)	5 (highest) (n = 97)	P^2	1 (lowest) (n = 98)	3 (n = 97)	5 (highest) (n = 97)	P^2
	mg/L				*mg/L*			
Crude	2.17 ± 2.22[3]	1.73 ± 2.11	1.48 ± 1.76	< 0.001	2.25 ± 2.19	1.69 ± 2.03	1.38 ± 1.95	< 0.001
Model 1[4]	1.94 ± 2.10	1.65 ± 1.86	1.56 ± 1.54	< 0.01	2.03 ± 2.01	1.58 ± 1.98	1.47 ± 1.89	< 0.001
Model 2[5]	1.91 ± 2.06	1.63 ± 1.81	1.58 ± 1.50	< 0.01	2.00 ± 1.99	1.55 ± 1.95	1.50 ± 1.86	< 0.01
Model 3[6]	1.89 ± 1.95	1.60 ± 1.70	1.61 ± 1.42	< 0.05	1.95 ± 1.91	1.51 ± 1.90	1.52 ± 1.76	< 0.01

[1] n = 486.
[2] ANCOVA.
[3] $\bar{x}$ ± SEM (all such values).
[4] Adjusted for age, BMI, and waist circumference.
[5] Additionally adjusted for smoking, physical activity, total energy intake, use of estrogen, menopausal status, and family history of diabetes or stroke.
[6] Additionally adjusted for energy from fat, cholesterol intake, meat and fish consumption, dairy intake, whole- and refined-grain intakes, and mutual effects of fruit and vegetable intakes.

association was observed between intake of fruit and a low HDL-cholesterol concentration.

Higher consumption of vegetables was also associated with a lower risk of metabolic syndrome features (**Figure 2**). In multivariate-adjusted models, subjects in the upper quintile of vegetable intake had lower odds of having the metabolic syndrome features. As for fruit, higher consumption of vegetables was not associated with prevalence of low HDL cholesterol. However, when fruit and vegetable intakes were considered together, we observed a marginally significant inverse association (odds ratio for quintile 5 versus quintile 1: 0.95; 95% CI: 0.85, 0.99; P = 0.046) with the prevalence of low HDL cholesterol.

DISCUSSION

In the current study we observed an inverse association of fruit and vegetable intakes with CRP. We also found that higher intakes of fruit and vegetable were associated with a lower risk of the metabolic syndrome. To our knowledge, this is the first study to directly relate fruit and vegetable intakes with the metabolic syndrome. Recently, 2 clinical trials (25, 35) and 2 observational studies (26, 36) have examined the association of fruit and vegetable intakes with CRP, but the participants were limited to men (25, 36) or the elderly (26) and such an association has not been observed in women. However, the beneficial effects of fruit and vegetable intakes in the framework of dietary patterns were reported previously, and it has been shown that dietary patterns rich in fruit and vegetables may reduce the risk of the metabolic syndrome (37, 38) and are associated with lower concentrations of inflammatory markers (39). We also have shown in a randomized clinical trial that consumption of a DASH (Dietary Approaches to Stop Hypertension) diet, ie, a diet rich in fruit and vegetables, has beneficial effects on features of the metabolic syndrome (40). Esposito et al (41) showed that the Mediterranean diet, which is rich in fruit and vegetables, lowers plasma markers of inflammation and endothelial dysfunction.

A favorable association of fruit and vegetable consumption with CRP and the metabolic syndrome may be attributed to the healthy lifestyle associated with higher intakes of these foods. However, the apparently protective effect of fruit and vegetable consumption persisted in multivariate models after known

Table 4
Multivariate-adjusted odds ratios (and 95% CIs) for the metabolic syndrome across quintiles of fruit and vegetable intakes

	Fruit quintiles				Vegetable quintiles			
Metabolic syndrome[1]	1 (lowest) (n = 98)	3 (n = 97)	5 (highest) (n = 97)	P for trend[2]	1 (lowest) (n = 98)	3 (n = 97)	5 (highest) (n = 97)	P for trend[2]
Model 1[3]	1.00	0.92 (0.80, 1.10)	0.58 (0.49, 0.86)	< 0.01	1.00	0.91 (0.83, 1.18)	0.62 (0.54, 0.83)	< 0.01
Model 2[4]	1.00	0.95 (0.81, 1.09)	0.63 (0.53, 0.82)	< 0.01	1.00	0.97 (0.85, 1.14)	0.68 (0.58, 0.84)	< 0.01
Model 3[5]	1.00	0.96 (0.82, 1.09)	0.66 (0.54, 0.80)	< 0.01	1.00	0.97 (0.86, 1.11)	0.70 (0.61, 0.84)	< 0.01
Model 4[6]	1.00	1.02 (0.93, 1.19)	0.89 (0.79, 1.02)	0.09	1.00	1.06 (0.95, 1.27)	0.86 (0.73, 0.99)	0.07

[1] Defined as the presence of ≥3 of the following components: *1*) abdominal adiposity (waist circumference > 88 cm), *2*) low serum HDL cholesterol (<50 mg/dL), *3*) high serum triacylglycerol (≥150 mg/dL), *4*) elevated blood pressure [≥130 (systolic)/85 (diastolic) mm Hg], and *5*) abnormal glucose homeostasis (fasting plasma glucose ≥110 mg/dL).
[2] Mantel-Haenszel extension chi-square test.
[3] Adjusted for age, energy intake, cholesterol intake, percentage of energy from fat, cigarette smoking, physical activity level, current estrogen use, menopausal status, and family history of diabetes or stroke.
[4] Additionally adjusted for intakes of whole grains, refined grains, dairy products, meat and fish, and mutual effects of fruit and vegetable intakes.
[5] Additionally adjusted for C-reactive protein concentrations.
[6] Additionally adjusted for BMI.

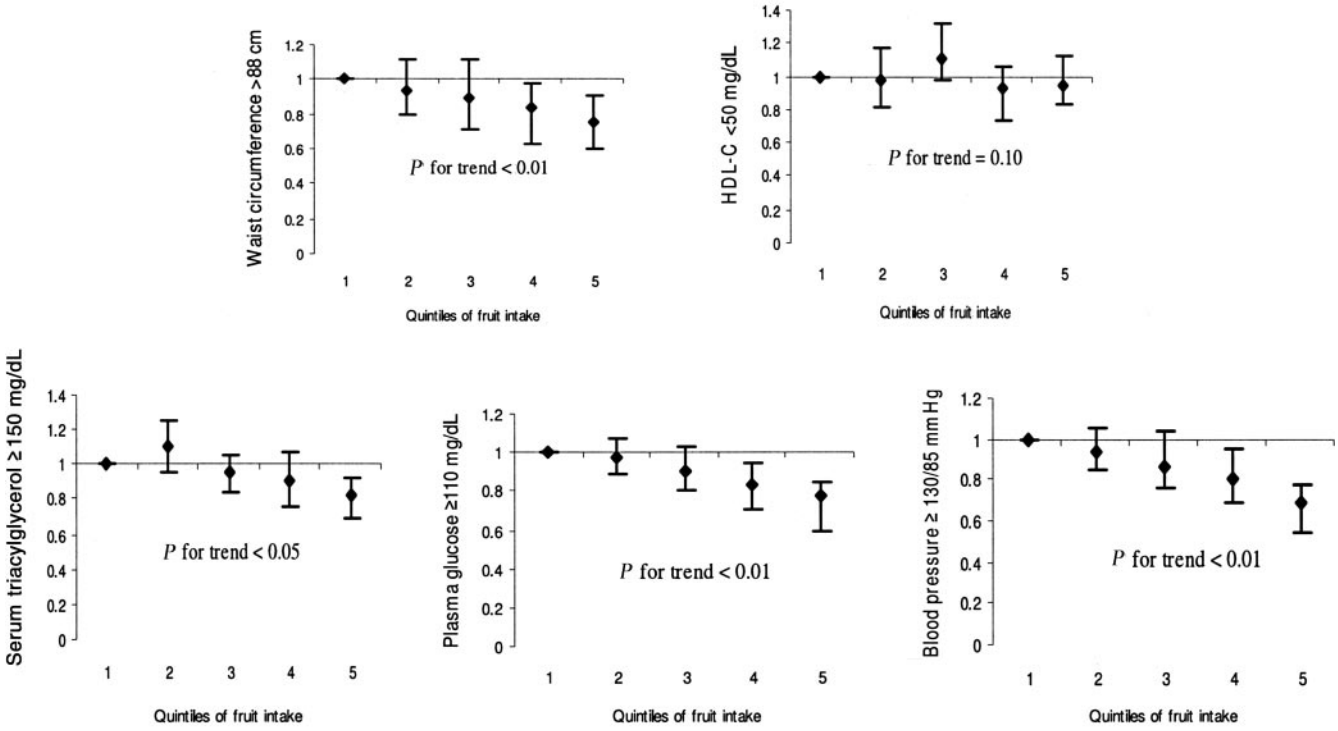

FIGURE 1. Multivariate-adjusted odds ratios and 95% CIs for features of the metabolic syndrome across quintiles of fruit intake. The odds ratios were adjusted for age, percentage of energy from fat, cigarette smoking, physical activity, current estrogen use, menopausal status, family history of diabetes or stroke, plasma concentrations of C-reactive protein, and intakes of whole grains, refined grains, dairy products, meat and fish, energy, and cholesterol. The number of participants was 97–98 in each quintile. *P* for trend values were derived with the Mantel-Haenszel extension chi-square test. HDL-C, HDL cholesterol.

potential confounders were accounted for. Second, some intermediary events, including dyslipidemia or elevated blood pressure, could have led to changes in diet and may therefore confound the association between fruit and vegetable intakes and the metabolic syndrome. However, such residual confounding effects would tend to attenuate the risk estimates toward the value of 1, because subjects with risk factors will be advised to follow a healthy diet rich in fruit and vegetables. Also, one may conclude that this association is a result of the participation of highly educated participants in our study. Although teachers in our community have a higher socioeconomic status than does the general Iranian population, the participants in our study have been selected from 4 large socioeconomically diverse districts of Tehran, which covers a broad range of dietary habits. Compared with other studies that have been reported from Iran (11, 12, 42, 43), this report covers a wide range of fruit and vegetable intakes. Given these characteristics, it is unlikely that the whole associations between fruit and vegetable intakes and the metabolic syndrome in our study could be explained by this type of bias. It is also possible that the participants in our study overestimated their intakes because of the relatively large number of questions used to assess intakes of fruit and vegetables (≈30 questions for fruit and 22 questions for vegetables) in our questionnaire. However, even if there was some overestimation of fruit and vegetable intakes, such overestimation is unlikely to bias the risk estimates.

Although the risk of both cardiovascular disease and type 2 diabetes is mediated in part by tissue sensitivity to the effects of insulin (44), no epidemiologic study has examined the association of fruit and vegetable intakes with the insulin resistance syndrome or the metabolic syndrome. In the current study, the prevalence and odds of having the metabolic syndrome were lower in those with a higher intake of fruit and vegetables. Our findings are in line with those of previous studies that have shown a protective effect of fruit and vegetable intakes against mortality (45), cardiovascular disease (18), and diabetes (46). Another cross-sectional study in young adults also showed that persons with the metabolic syndrome have significantly lower intakes of fruit and vegetables than do those with no metabolic risks (47). A portion of these cardioprotective effects of fruit and vegetable intakes may be mediated through the effect of their components (eg, antioxidants) on inflammatory markers (23, 36). However, few studies have related fruit and vegetable consumption to markers of inflammation, particularly in women. We showed that a higher consumption of fruit and vegetables is associated with lower plasma concentrations of CRP. Although this favorable apparent effect of fruit and vegetable intakes was observed in another epidemiologic study in a Hispanic elderly population (26), the results of clinical trials are not consistent. Watzl et al (25), in a 4-wk randomized controlled clinical trial in healthy nonsmoking men, showed that consumption of 8 daily servings of carotenoid-rich fruit and vegetables significantly reduced plasma CRP concentrations compared with those who consumed 2 daily servings. In contrast, Freese et al (35), in a 6-wk randomized controlled study of healthy subjects aged 19–52 y, observed no difference in inflammatory markers, including CRP, between those who consumed a diet providing 810 g fruit and vegetables per 10 MJ (2390 kcal) and those who consumed an isocaloric diet providing 196 g fruit and vegetables per 10 MJ (2390 kcal). However, although the interpretation of these intervention studies is complicated by the different age ranges of the subjects

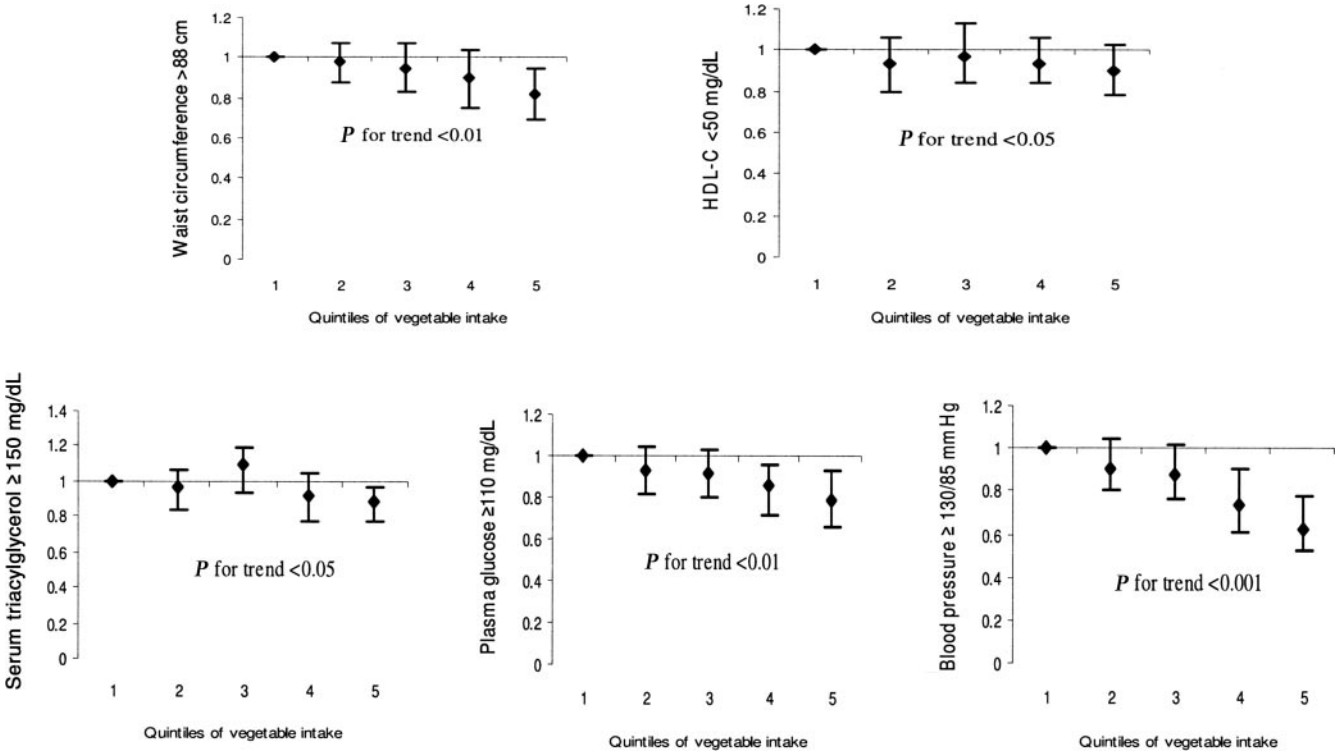

FIGURE 2. Multivariate-adjusted odds ratios and 95% CIs for features of the metabolic syndrome across quintiles of vegetable intake. The odds ratios were adjusted for age, percentage of energy from fat, cigarette smoking, physical activity, current estrogen use, menopausal status, family history of diabetes or stroke, plasma concentrations of C-reactive protein, and intakes of whole grains, refined grains, dairy products, meat and fish, energy, and cholesterol. The number of participants was 97–98 in each quintile. *P* for trend values were derived with the Mantel-Haenszel extension chi-square test. HDL-C, HDL cholesterol.

studied and by the short duration of the interventions, it appears that the long-term consumption of fruit and vegetables is more important than is the short-term consumption of these foods on the modulation of markers of inflammation.

Eating ≥5 servings of fruit and vegetables daily is recommended to reduce the risk of chronic diseases (48). Data from the National Food Consumption Survey in Iran have shown lower intakes of fruit and vegetables by Iranians than those recommended (42). In the current study, subjects in the top quintile of fruit and vegetable intake consumed 362 g fruit/d and 279 g vegetables/d. The mean fruit and vegetable intakes in our study were 228 and 186 g/d, respectively; these intakes are higher than those reported form Finland in The Seven Countries Study (49) and lower than those reported for American men in the Nutrition Status Survey in Massachusetts (50). In the Health Professionals Follow-Up Study and the Nurses' Health Study (51) and in the Framingham Heart Study (52), the intake of fruit and vegetables was ≈5 servings/d and in the Women's Health Study the intake was 6 servings/d (18). However, it should be kept in mind that some of these studies, like our study, did not include potato in the vegetable group (52). Considering the favorable association of fruit and vegetable consumption with the metabolic syndrome and inflammatory markers, it seems likely that an increased consumption of these products will considerably reduce the risk of metabolic disorders.

Our findings need to be interpreted while considering some limitations. First, we used cross-sectional data to assess the association of fruit and vegetable intakes with the metabolic syndrome. Although a direct prospective association between fruit and vegetable intakes and the metabolic syndrome has not yet been reported, many studies have shown a prospective association between fruit and vegetable intakes and risk factors related to the metabolic syndrome. Second, because we used an FFQ to assess dietary intakes, misclassification was a major concern in our study, as it is in all epidemiologic studies. Third, diets rich in fruit and vegetables were associated with a healthier lifestyle, which may not have been accurately captured and controlled in our analysis and, thus, may have resulted in residual confounding. Fourth, the risk estimates obtained in our study were not adjusted for glycemic load, a dietary agent that has been shown to correlate with both CRP (53) and the metabolic syndrome (54). However, the associations we observed were unlikely to be confounded significantly by dietary glycemic load because the extensive adjustments we made had minimal effects on the odds ratios. Fifth, subjects with known chronic diseases were excluded from the study. These exclusions may have reduced the likelihood of finding significant trends in the odds of having metabolic risks across quintile categories of fruit and vegetable consumption. Sixth, this study included only women. Iranian women behave differently with metabolic syndrome than do men. The prevalence of the metabolic syndrome among women in Iran is almost twice that in men (8) and, of all women in the world, Iranian women have the highest prevalence (3). Seventh, we did not include potato in the vegetable group because recent studies have shown that potato consumption can increase the risk of diabetes (55); therefore, recommendations to include potatoes as a vegetable may not be warranted (26). However, inclusion of

potato as a vegetable in this study attenuated the associations but they remained significant.

In conclusion, this study showed that higher intakes of fruit and vegetables were associated with a lower risk of the metabolic syndrome; the lower risk may be the result of lower CRP concentrations. These findings support current dietary recommendations to increase intakes of fruit and vegetables as a primary preventive measure against cardiovascular disease. Our results also provide further evidence for the hypothesis that a high intake of fruit and vegetables is associated with reduced plasma concentrations of inflammatory markers.

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AE and LA designed the study, collected and analyzed the data, and wrote the manuscript. MK supervised the research. YM served as an advisor for the research. FBH and WCW commented on this work and helped prepare the manuscript.

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