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Fruit and vegetable consumption and risk factors for cardiovascular disease

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Abstract

The international guidelines issued by the World Health Organization recommend reduction in dietary saturated fat and cholesterol intakes as means to prevent hypercholesterolemia and cardiovascular disease (CVD); however, only limited data are available on the benefits of fruit and vegetable consumption on CVD risk factors in a community-based population. The aim of this study was to examine whether, and to what extent, intake of fruits and vegetables is inversely associated with CVD risk factors in adults. In this population-based cross-sectional study, a representative sample of 840 Tehranian adults (male and female) aged 18 to 74 years was randomly selected in 1998. Multivariate logistic regression adjusted for lifestyle and nutritional confounders was used in 2 models. After adjusting for confounders, dietary fruit and vegetable were found to be significantly and inversely associated with CVD risk factors. Adjusted odds ratio for high low-density lipoprotein concentrations were 1.00, 0.88, 0.81, and 0.75 (P for trend < .01) in the first model, which was adjusted for age, sex, keys score, body mass index, energy intake, smoking status, dietary cholesterol, and history of diabetes mellitus and coronary artery disease, a trend which was not appreciably altered by additional adjustment for education, physical activity, and saturated, polyunsaturated, and total fat intakes. This association was observed across categories of smoking status, physical activity, and tertiles of the Keys score. Exclusion of subjects with prevalent diabetes mellitus or coronary artery disease did not alter these results significantly. Consumption of fruits and vegetables is associated with lower concentrations of total and low-density lipoprotein cholesterol and with the risk of CVD per se in a dose-response manner.
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1. Introduction

Cardiovascular diseases (CVDs) are among the most common causes of death and disability worldwide [1]. The risk of CVD rises with increasing age, body weight, blood pressure, cigarette smoking, alcohol intake, and dyslipidemia [2,3]. Epidemiologic studies have shown that elevated concentrations of serum total cholesterol and low-density lipoprotein cholesterol (LDL-C) are independent risk factors for CVD [4,5]. Plasma concentrations of LDL and other risk factors of CVD are influenced by both genetic and environmental factors. Although it is difficult to alter genetic factors, modifiable environmental factors such as smoking or dietary patterns could be targeted in preventive interventions aimed at lowering these risk factors.

The standard international guidelines issued by the World Health Organization [6] recommend reductions in dietary saturated fat and cholesterol intakes as means to prevent hypercholesterolemia; however, only limited data are available on the benefits of fruit and vegetable consumption on CVD risk factors in a community-based population. Data on the effects of fruit and vegetable intakes on LDL are inconsistent. In the Dietary Approaches to Stop Hypertension trial [7], a diet high in fruits and vegetables was not associated with a significant reduction in LDL compared with the control diet, although the trend suggests a decrease in plasma LDL concentrations. In contrast, in other studies [8], fruit and vegetable consumption decreased LDL concentration in hypercholesterolemic subjects.

In the current study, we evaluated whether higher intakes of fruits and vegetables could be inversely related to CVD risk factors.

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2. Methods

2.1. Subjects

The current study is a cross-sectional study conducted within the framework of the Tehran Lipid and Glucose Study (TLGS), a prospective study of a representative sample of residents of district 13 of Tehran, performed with the aim of ascertaining the prevalence of noncommunicable disease risk factors and developing a healthy lifestyle to curtail these risk factors [9]. Tehran, the capital of Iran, is a metropolitan city (with a population of about 12 million) composed of 20 urban districts, including district 13 in the eastern part of the city. District 13 was chosen for the study for 2 reasons: (1) the high stability of the population residing in this district and (2) the age distribution of this district being representative of Tehran's population. In a previous study, we showed that the TLGS provides a representative sample of the urban population of Tehran [9]. In the TLGS, 15005 persons aged at least 3 years were selected by a multistage cluster, random sampling method; and a representative sample of 1476 persons was randomly selected for dietary assessment, including 861 subjects aged 18 to 74 years. Data were collected in 1998. In the current population-based cohort study, we also excluded subjects whose reported daily energy intakes were outside the range of 800 to 4200 kcal/d (3347-17 573 kJ/d) [10]. Therefore, 840 subjects (361men and 479 women), aged 18 to 74 years, remained for the current analysis. Each subject provided written informed consent, and the protocol of this study was approved by the research council of The Endocrine Research Center of Shahid Beheshti University (M.C.).

2.2. Measurements

While subjects were minimally clothed and not wearing shoes, weight was measured with the use of digital scales (Seca 707, Hanover, MD) and recorded to the nearest 100 g. Height was measured with a tape measure while the subjects were in a standing position with the shoulders in a normal resting state and not wearing shoes and recorded to the nearest centimeter (Seca 208 Portable Body Meter Measuring Device). Body mass index (BMI) was calculated as body mass (weight) in kilograms divided by height in meters squared. Measurements were recorded to the nearest 0.1 cm, as reported earlier [11]. To reduce subjective error, all measurements were taken by the same male physician for all men and the same female physician for all women. There was significant correlation between the test and retest results taken by the male and female physicians (r >0.75, P < .01 for both).

Physical activity level was determined using the Lipid Research Clinics questionnaire [12], which is a simple and comprehensible measure including 4 questions; no special education is needed to complete this questionnaire, according to which individuals are divided into 3 groups of light, moderate, and heavy physical activity. Blood pressure was measured twice after the participants sat for 15 minutes [13]. Additional covariate information about age, smoking habits [14], medical history, and current use of medications [14] was obtained with the use of validated questionnaires, as reported earlier. Fasting blood samples were drawn for the measurement of glucose and lipid concentrations after overnight fast of 12 hours [15].

Usual dietary intake was assessed with the use of a 168-item semiquantitative food frequency questionnaire (FFQ). All the questionnaires were administered by trained dietitians who had more than 5 years of experience in the Nationwide Food Consumption Survey project [16,17]. The FFQ consisted of a list of foods with a standard serving size. Participants were asked to report their frequency of consumption of each food item during the previous year on a daily (eg, bread), weekly (eg, rice, meat), or monthly (eg, fish) basis. Portion sizes of consumed foods were converted from household measures to grams [18]. Each food and beverage were then coded according to the prescribed protocol and analyzed for content of energy and the other nutrients by using Nutritionist III software (version 7.0; N-Squared Computing, Salem, OR), designed for Iranian foods.

The reliability of the FFQ in this cohort was evaluated in a randomly chosen subgroup of 132 subjects by comparing nutrient consumption ascertained by FFQ responses on 2 separate occasions. The correlation coefficients for the repeatability of grain, vegetables, fruits, dairy, and meat were 0.85, 0.79, 0.71, 0.74, and 0.70, respectively. The FFQ also had high reliability for nutrients; for example, the correlation coefficient was 0.81 for dietary fiber. For fruit consumption, each participant was asked how often, on average, he or she consumed fruit such as apples, orange, bananas, peaches, grapes, strawberries, pears, watermelon, grapefruit, prunes, pomegranates, kiwi, persimmons, raisins, figs, coconuts, apricots, sweet lemon, and lemon during the previous year. For vegetable consumption, subjects were asked about their average consumption of vegetables such as onions, cucumbers, lettuces, carrots, cauliflower, Brussels sprouts, kale, cabbage, spinach, mixed vegetables, corn, green beans, green peas, peppers, beets, potatoes, tomatoes, broccoli, and celery. Response categories ranged from almost never, 1 to 3/mo, 1/wk, 2 to 4/wk, 5 to 6/wk, 1/d, 2 to 3/d, 4 to 6/d, to more than 6/d. The portion size of each fruit and vegetable was specified to facilitate determination of the number of typical servings and nutrient content. Comparative validity was determined by comparison of FFQ data with intake estimated from the average of twelve 24-hour dietary recalls (one for each month of the year). Preliminary analysis of the validation study showed that nutrients commonly found in fruits and vegetables were moderately correlated using these 2 methods after controlling for total energy intake. 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 fruits and 0.57 for vegetables. Overall, these data indicate that the FFQ provides reasonably valid measures of the average long-term dietary intakes.

Blood glucose was measured on the day of blood collection using the enzymatic colorimetric method with glucose oxidase. Glucose tolerance status was classified according to the World Health Organization criteria as normal glucose tolerance, impaired glucose tolerance, or diabetes [19]. Serum concentrations of total cholesterol and triglyceride (TG) were measured by using commercially available enzymatic reagents (Pars Azmoon, Tehran, Iran) adapted to the Selecta auto analyzer (Vital Scientific, Spankeren, the Netherlands). High-density lipoprotein cholesterol (HDL-C) was measured after precipitation of the apolipoprotein B–containing lipoproteins with phosphotungstic acid. Low-density lipoprotein cholesterol was calculated according to the method of Friedewald et al [20]. It was not calculated when serum concentration of TG was greater than 400 mg/dL. All samples were analyzed when internal quality control met the acceptable criteria. Interassay and intraassay coefficients of variation were 2% and 0.5% for total cholesterol and 1.6% and 0.6% for TG, respectively.

The Rose questionnaires [21] on chest pain were completed for all participants, and Minnesota code of a 12-lead electrocardiogram [22] was taken. The prevalence of coronary artery disease (CAD) based on its presence according to the Rose questionnaires or electrocardiogram or both of them was calculated.

2.3. Definition of terms

Cardiovascular risk factors were defined as follows: (1) high total cholesterol (≥240 mg/dL), (2) high serum LDL-C (>130 mg/dL), (3) low serum HDL-C (<40 mg/dL for men and <50 mg/dL for women), (4) high serum TG concentrations (≥200 mg/dL), (5) elevated systolic (≥140 mmHg) or diastolic (≥90 mmHg) blood pressure, (6) abnormal glucose homeostasis (fasting plasma glucose concentration ≥110 mg/dL), and (7) high BMI (>30 kg/m^2) [23-26].

2.4. Statistical analysis

We used SPSS software (version 9.05; SPSS, Chicago, IL) for all statistical analyses. Dietary recommendations are graphically represented by a food pyramid consisting of 5 shelves. There is a recommended number of servings per day from each shelf that together combine to give an overall healthy and nutritious diet for the general adult population [27]. The second shelf relates to fruits and vegetables, of which 4 or more servings per day are recommended; subjects were hence categorized based on category cut points: 0 to 1.9, 2 to 2.9, 3.0 to 3.9, and at least 4 servings per day. Significant differences in general characteristics across categories of fruit and vegetable intakes were searched using 1-way analysis of variance, and *P* for differences was calculated. Besides, *P* for regression (fruit and vegetable intake as independent variable) was calculated. Food intakes were adjusted for age, sex, and total energy intake. The χ^2 test was used to detect any significant differences in the distribution of subjects across categories of fruit and vegetable intake with regard to qualitative variables. We used a general linear model to estimate adjusted mean concentrations of CVD risk factors across categories of fruit and vegetable intakes. Adjustment was made for age, sex, Keys score [28], BMI, energy intake, smoking status (never, former, and current smokers), dietary cholesterol, history of CAD, diabetes

Table 1
Characteristics of TLGS participants by categories of fruit and vegetable intakes

Variables	Categories of fruit and vegetable intake				P^a
	1 (n = 140)	2 (n = 190)	3 (n = 220)	4 (n = 290)	
Men (%)	43.1	43.5	42.7	48.8	.54
Age (y)	37.4 ± 14.0[b]	37.9 ± 14.5	36.8 ± 12.8	36.4 ± 12.6	.50
BMI (kg/m^2)	25.7 ± 4.8	25.6 ± 5.2	26.3 ± 4.9	26.0 ± 4.9	.43
Keys score[c]	48.2 ± 4.8	43.4 ± 8.9	41.4 ± 8.0	37.5 ± 7.9	<.01
Physical activity (%)					
Light	57	57	58	56	.81
Moderate	30	31	30	32	.77
Heavy	13	12	12	12	.77
College education (%)	12	13	17	19	<.01
Current smoking (%)	13	10	10	5	<.04
CAD[d] (%)	*23.5*	*18.1*	*15.2*	*11.4*	<.01
Diabetes mellitus (%)	2.3	3.0	3.5	2.5	.70
Cholesterol-lowering medication (%)	9	8	7	8	.63

Cutoffs were 0 to 1.9, 2 to 2.9, 3.0 to 3.9, and at least 4 servings per day for fruit and vegetable categories 1 to 4, respectively.

[a] *P* for difference among fruit and vegetable categories (analysis of variance test for data that are mean ± SD and χ^2 for data that are percentages).

[b] Mean ± SD (all such values).

[c] Calculated as $1.35(2S - P) + 1.5\sqrt{C}$, where *S* and *P* are percentages of energy from saturated fat and polyunsaturated fat, respectively, and *C* is dietary cholesterol in milligrams per 1000 kcal.

[d] Coronary artery disease.

Table 2
Dietary intakes of our participants of the TLGS across categories of fruit and vegetable intakes

Variables	Categories of fruit and vegetable intake				P^a	P for regression
	1 (n = 140)	2 (n = 190)	3 (n = 220)	4 (n = 290)		
Energy (kcal/d)	2118 ± 15[b]	2313 ± 13	2505 ± 11	2672 ± 10	<.01	<.01
Total protein						
(g/d)	60 ± 4	67 ± 4	72 ± 6	76 ± 5	<.01	<.01
(% of energy)	10.0 ± 1.1	11.6 ± 1.8	11.5 ± 1.1	11.3 ± 1.8	.89	.76
Total carbohydrate						
(g/d)	270 ± 10	316 ± 9	360 ± 9	395 ± 10	<.01	<.01
(% of energy)	55.4 ± 1	54.8 ± 1	57.2 ± 1	59.2 ± 1	<.01	.15
Total dietary fiber (g/d)	4.2 ± 0.9	6.1 ± 1.4	11.1 ± 1.6	19.2 ± 1.4	<.01	<.01
Total fat						
(g/d)	80 ± 7	86 ± 6	87 ± 6	74 ± 6	<.01	.32
(% of energy)	34.4 ± 3.0	33.5 ± 4.9	31.4 ± 3.3	29.4 ± 4.1	<.03	<.02
SFA						
(g/d)	34.5 ± 2.8	32.3 ± 3.5	33.6 ± 3.3	31.4 ± 3.4	.20	.30
(% of energy)	14.7 ± 2.4	12.6 ± 2.1	12.1 ± 2.0	10.6 ± 2.2	<.04	<.03
MUFA						
(g/d)	28.0 ± 3.3	27.4 ± 3.4	27.8 ± 3.5	26.1 ± 3.5	.10	.10
(% of energy)	11.9 ± 2.3	10.7 ± 2.0	10.0 ± 2.2	8.8 ± 2.1	.27	.07
PUFA						
(g/d)	8.0 ± 1.2	8.2 ± 1.4	8.6 ± 1.9	7.1 ± 1.6	.08	.18
(% of energy)	3.4 ± 0.9	3.2 ± 0.4	3.1 ± 0.7	2.4 ± 0.5	<.01	<.01
Dietary cholesterol (mg/d)	155 ± 5	170 ± 5	189 ± 4	173 ± 4	.12	.12
Vitamin C (mg/d)	56 ± 4	83 ± 4	112 ± 4	145 ± 4	<.01	<.01
Potassium (mg/d)	433 ± 11	527 ± 11	857 ± 10	1912 ± 10	<.01	<.01

SFA indicates saturated fatty acid; MUFA, monounsaturated fatty acid; PUFA, polyunsaturated fatty acid.
[a] P for differences among fruit and vegetable categories (analysis of covariance).
[b] All values are mean ± SEM. Reported means of nutrient and food intakes were adjusted for age, sex, and total energy intake.

mellitus, education (high school graduate or less, vocational school, and college or more), physical activity (light, moderate, heavy), total fat, saturated fat, and polyunsaturated fat.

The Keys score correlates changes in fatty acid intake with changes in serum cholesterol and is computed as follows: Keys score = $1.35(2S - P) + 1.5\sqrt{C}$ [28], where S and P are percentages of energy from saturated fat and polyunsaturated fat, respectively, and C is dietary cholesterol in milligrams per 1000 kcal. Therefore, in secondary analyses, we conducted stratified analyses according to sex, tertiles of Keys score, smoking status (current nonsmokers and current smokers), and college education (yes, no). Furthermore, we repeated the analyses after excluding 159 subjects (n = 20 with diabetes mellitus, n = 120 with CAD, and n = 19 with both diseases). To ascertain the association of fruit and vegetable intakes with CVD risks, we used multivariable logistic regression in 2 models, with

Table 3
Multivariate adjusted means for CVD risk factors across categories of fruit and vegetable intakes

Variables	Categories of fruit and vegetable intake				P^a	P for regression
	1 (n = 140)	2 (n = 190)	3 (n = 220)	4 (n = 290)		
BMI (kg/m^2)	25.7 ± 4.8	25.6 ± 0.3	26.3 ± 0.3	26.0 ± 0.3	.43	.76
Total cholesterol (mg/dL)	225 ± 3	210 ± 3	197 ± 3	178 ± 3	<.03	<.03
LDL-C (mg/dL)	130 ± 2	120 ± 3	110 ± 4	95 ± 2	<.01	<.01
HDL-C (mg/dL)	44 ± 0.8	43 ± 0.8	43 ± 0.8	44 ± 0.8	.96	.87
TG (mg/dL)	138 ± 4	148 ± 6	143 ± 6	139 ± 4	.56	.66
Total cholesterol to HDL-C	5.3 ± 0.1	5.0 ± 0.1	4.6 ± 0.1	3.7 ± 0.1	<.04	<.03
LDL-C/HDL-C	3.1 ± 0.1	2.9 ± 0.1	2.6 ± 0.1	2.3 ± 0.1	<.02	<.03
Fasting plasma glucose (mg/dL)	92 ± 1	89 ± 0.8	96 ± 2	92 ± 1	.90	.80
Systolic blood pressure (mm Hg)	114 ± 1	115 ± 1	115 ± 1	117 ± 1	.78	.48
Diastolic blood pressure (mm Hg)	77 ± 0.8	77 ± 0.7	77 ± 0.8	77 ± 0.7	.77	.78

All values are mean ± SEM after adjustment for age, sex, Keys score [28], BMI, energy intake, smoking status, dietary cholesterol, history of CAD, diabetes mellitus, education, physical activity, total fat, saturated fat, and polyunsaturated fat.
[a] P for difference among categories (analysis of covariance).

Table 4
Distribution of subjects with CVD risk factors across different categories of fruit and vegetable intakes

Variables	Categories of fruit and vegetable intake				P
	1 (n = 140)	2 (n = 190)	3 (n = 220)	4 (n = 290)	
BMI >30 kg/m^2	20.2	19.0	20.9	19.8	.97
Total cholesterol ≥240 mg/dL	18.6	17.1	14.1	13.2	.09
LDL-C >130 mg/dL	48.0	44.0	42.1	39.0	.04
Low HDL-C[a]	15.5	20.3	18.2	16.2	.69
TG ≥200 mg/dL	19.2	23.6	19.7	19.2	.61
Fasting plasma glucose ≥110 mg/dL	4.2	6.6	4.5	6.2	.67
Systolic blood pressure ≥140 mm Hg	6.1	7.0	6.5	6.1	.85
Diastolic blood pressure ≥90 mm Hg	7.5	10.7	10.1	10.6	.34

[a] Defined as less than 40 mg/dL for men and less than 50 mg/dL for women.

the first model controlled for age, sex, Keys score, BMI, energy intake, smoking status (never, former, and current smokers), dietary cholesterol, history of CAD, and diabetes mellitus and the second model for education (high school graduate or less, vocational school, and college or more), physical activity (light, moderate, heavy), total fat, saturated fat, and polyunsaturated fat in addition to the factors in the first model.

Table 5
Multivariate adjusted odds ratios (and 95% confidence intervals) for CVD risk factors across categories of fruit and vegetable intakes

	Categories of fruit and vegetable intake				P for trend
	1 (n = 140)	2 (n = 190)	3 (n = 220)	4 (n = 290)	
High BMI[a]					
Model 1[b]	1.00	0.91 (0.79-1.08)[c]	1.13 (0.90-1.27)	0.96 (0.81-1.13)	NS
Model 2[d]	1.00	0.98 (0.83-1.13)	1.13 (0.90-1.27)	0.91 (0.79-1.08)	NS
High total cholesterol[e]					
Model 1	1.00	0.89 (0.76-1.02)	0.77 (0.69-0.89)	0.70 (0.59-0.89)	<.02
Model 2	1.00	0.95 (0.80-1.10)	0.89 (0.79-1.08)	0.82 (0.70-0.98)	<.05
High LDL-C[f]					
Model 1	1.00	0.88 (0.75-0.94)	0.81 (0.68-0.98)	0.75 (0.59-0.89)	<.01
Model 2	1.00	0.91 (0.79-1.08)	0.86 (0.69-1.05)	0.79 (0.63-0.96)	<.02
Low HDL-C[g]					
Model 1	1.00	1.25 (1.05-1.38)	1.12 (0.94-1.22)	1.03 (0.89-1.18)	NS
Model 2	1.00	1.20 (1.02-1.33)	1.16 (1.00-1.33)	1.08 (0.91-1.21)	NS
High TG[h]					
Model 1	1.00	1.17 (1.01-1.32)	1.13 (0.91-1.22)	1.02 (0.87-1.14)	NS
Model 2	1.00	1.20 (1.02-1.33)	1.15 (1.02-1.31)	1.07 (0.90-1.20)	NS
High fasting plasma glucose[i]					
Model 1	1.00	1.40 (1.23-1.61)	0.92 (0.80-1.07)	1.30 (1.17-1.41)	NS
Model 2	1.00	0.72 (0.69-0.89)	1.84 (0.74-1.05)	0.71 (0.57-0.89)	NS
High systolic blood pressure[j]					
Model 1	1.00	1.01 (0.89-1.18)	1.12 (0.91-1.22)	1.02 (0.89-1.18)	NS
Model 2	1.00	1.05 (0.89-1.19)	1.14 (0.92-1.26)	1.03 (0.90-1.21)	NS
High diastolic blood pressure[k]					
Model 1	1.00	1.20 (1.02-1.33)	1.11 (0.96-1.29)	1.20 (1.02-1.33)	NS
Model 2	1.00	1.20 (1.02-1.33)	1.12 (0.96-1.29)	1.22 (1.03-1.37)	NS

NS indicates not significant.
[a] Defined as greater than 30 kg/m^2.
[b] Model 1 was adjusted for age, sex, Keys score, BMI, energy intake, smoking status (never, former, and current smokers), dietary cholesterol, history of CAD, and diabetes mellitus.
[c] Data are odds ratio (95% confidence interval).
[d] Model 2 additionally adjusted for education (high school graduate or less, vocational school, and college or more), physical activity (light, moderate, heavy), total fat, saturated fat, and polyunsaturated fat.
[e] Defined as at least 240 mg/dL.
[f] Defined as greater than 130 mg/dL.
[g] Defined as less than 40 mg/dL for men and less than 50 mg/dL for women.
[h] Defined as at least 200 mg/dL.
[i] Defined as at least 110 mg/dL.
[j] Defined as at least 140 mmHg systolic.
[k] Defined as at least 90 mmHg diastolic.

3. Results

The study consisted of 840 subjects between 18 and 74 years of age; of these 840 subjects, 44.5% were men. The average age of participants was 37.2 ± 13.5 years (range, 18-74 years). Mean consumption of fruit and vegetables was 5.6 ± 3.4 servings per day (range, 0.5-19.8 servings per day). The mean and SDs of age and BMI as well as the distribution of subjects with regard to college education, diabetes mellitus, CAD, smoking, and physical activity status across categories of fruit and vegetable consumption are shown in Table 1. No significant differences were observed between the age of participants in category 1 (the lowest category) and those in category 4 of fruit and vegetable intake. Most subjects had light activity in all categories of fruit and vegetable intake. Subjects in upper categories of fruit and vegetable intake were less likely to be daily smokers compared with the other categories ($P < .04$). Higher intake of fruit and vegetable products was associated with lower prevalence of CAD ($P < .01$), higher educational attainment ($P < .01$), and lower Keys score ($P < .01$).

Table 2 shows age, sex, and total energy intake and adjusted dietary intakes of our population across categories of fruit and vegetable intake. Subjects in category 4 consumed more fiber than did subjects in the other categories. A higher intake of fruit and vegetable was associated with a healthier diet and also higher energy intake ($P < .01$), higher percentage of energy intake from carbohydrate, higher intake of potassium and vitamin C, and lower percentage of energy from total ($P < .05$) and saturated fat ($P < .04$).

Multivariate-adjusted means for blood pressure and serum lipid risk factors across categories of fruit and vegetable intake are presented in Table 3. Subjects in the upper category of fruit and vegetable intake had lower total cholesterol, LDL-C, total cholesterol to HDL-C, and LDL-C/HDL-C as compared with those in the lower category. No significant differences were observed between TG, fasting plasma glucose, HDL, and blood pressure of participants in category 1 (the lowest category) and those in category 4 of fruit and vegetable intake.

The distribution of subjects according to serum lipid risk factors in different categories of fruit and vegetable is shown in Table 4. The frequency of high LDL-C was the highest in category 1 of fruit and vegetable consumption. To assess residual confounding by dietary fat intake, we stratified by tertiles of Keys score. From the lowest to the highest category of fruit and vegetable consumption, multivariate-adjusted mean (±SE) for LDL-C concentrations were 128 ± 2, 118 ± 3, 109 ± 3, and 95 ± 4 mg/dL, respectively, for the lowest tertile of Keys score ($P < .04$); these values were 130 ± 2, 120 ± 3, 109 ± 3, and 93 ± 4 mg/dL, respectively, for the second tertile of Keys score ($P < .02$); and they were 128 ± 2, 120 ± 3, 110 ± 3, and 97 ± 4 mg/dL, respectively, for the third tertile of Keys score ($P < .04$). In addition, when stratified by sex, smoking status, and education, the relation between fruit and vegetable intakes and LDL-C concentrations persisted (data not shown).

Multivariate-adjusted odds ratios for the presence of cardiovascular risk factors across categories of fruit and vegetable intake are shown in Table 5. In categories 1 to 4 of fruit and vegetables, adjusted odds ratios for high LDL concentrations were 0.88, 0.81, and 0.75 (P for trend < .01) in the first model, which we adjusted for age, sex, Keys score, BMI, energy intake, smoking status (never, former, and current smokers), dietary cholesterol, history of CAD, and diabetes mellitus (Table 5). Additional adjustment for education, physical activity, and saturated, polyunsaturated, and total fat intakes did not alter the results. We repeated the analysis with quartiles of fruit and vegetable intake; and although results were not exactly the same, P for trend for total cholesterol and LDL-C between quartiles remained unchanged (data not shown).

4. Discussion

In this cross-sectional study, conducted in a group of Tehranian inhabitants, we found that consumption of fruit and vegetables was inversely related to total cholesterol and LDL-C concentrations, independent of age, sex, Keys score, smoking status, exercise, and educational attainment. Subjects in the highest fruit and vegetable intake groups had LDL-C and total cholesterol concentrations lower than those in the lowest fruit and vegetable intake groups. On the other hand, there was no significant difference in serum TG or HDL-C levels between participants in fruit and vegetable categories. Thus, the lower total cholesterol in participants with higher intake of fruit and vegetable was due to lower LDL-C levels, leading to a decrease in the atherogenic index (total cholesterol to HDL-C ratio) [29–31] and LDL-C/HDL-C ratio.

Although several clinical trials and observational studies have assessed the effects of dietary fat on LDL concentrations, limited data are available on the association between the consumption of fruit and vegetables and LDL concentrations in a community-based population. The Food and Drug Administration was one of the first national agencies to recognize a role for fiber in CVD risk reduction. Products that contain 0.75 g β-glucan or 1.78 g psyllium per serving are permitted to carry a health claim stating that the product will reduce the risk of coronary heart disease [32,33]. The Food and Drug Administration further determined that 4 servings of these foods are likely to provide the effective daily dose [32,33].

It is not clear in this study which constituents in fruit and vegetable may have potential hypocholesterolemic action. Generally, the effects of vegetables and fruits on cholesterol metabolism are attributed to their fiber content. Isolated dietary fiber from these plants such as pectins (12-50 g/d) [34], guar gum (10-20 g/d) [35], and psyllium (6-15 g/d)

[36] have been shown to lower cholesterol levels in humans. Studies of vegetarian diets have attributed some of the cholesterol lowering specifically to the pectin component of soluble fiber found in fruits and vegetables [34] because this soluble viscous fiber has been shown to lower serum cholesterol [37]. Viscous fibers increase fecal bile acid losses [38] and chenodeoxycholic acid synthesis [36], and appear to be the best substantial mechanisms by which fiber lowers serum cholesterol [39]. Very large losses of fecal bile acids on the vegetable diet may therefore have been related, in part, to pectin fiber content of the diet [34] or the sheer bulk of food passing through the gastrointestinal tract. Increased chenodeoxycholate and cholate synthesis rates were seen on the vegetable diet. The resulting reduction in hepatic cellular cholesterol concentration would lead to up-regulation of the LDL receptor, increased hepatic cholesterol uptake, and reduction in serum levels as observed.

Diets rich in fruit and vegetables are good sources of dietary fiber. In a randomized trial, a fiber-multivitamin combination resulted in a reduction in LDL-C of 8% from baseline after 8 weeks [40]. Other epidemiologic studies [41,42] and a meta-analysis [43] showed LDL-C–lowering effects of dietary fiber.

The absence of any difference in BMI between 4 categories despite higher calorie intake in upper categories may be explained by higher intakes of fruit and vegetables as well as total fiber, as Murakami et al [44] showed that dietary fiber intake has an independent negative association with BMI. So, we would expect lower BMI in the last category of fruit and vegetable if energy intakes of our participants were equal among 4 categories.

This study did not find any effect on blood pressure. In contrast, in previous study of Appel et al [45], systolic blood pressure was 2% lower in a fruit and vegetable group in comparison with a control group; diastolic blood pressure was 1.3% lower. Furthermore, randomized controlled trials have confirmed that a vegetarian diet, including a high amount of fruit and vegetable consumption, could also lower blood pressure [46,47]. Our study did not have sufficient statistical power to distinguish such small differences. The absence of a significant difference between blood pressure of the groups in our study could thus be explained by the number of participants or the cross-sectional design of the study, which was not specifically designed to test a blood pressure hypothesis. The composition of the diets however may be a more likely explanation. The differences in the amount of potassium between the low and high vegetable and fruit groups were much higher in the trial of Appel et al [45] in comparison with the amounts in our study (1700 and 4700 mg for both diets, respectively). Vitamin C is another compound that could have an effect on blood pressure [48]. In our study, the high group had much higher intakes of vitamin C in comparison with the low groups; but no effects on blood pressure were found. Trials on vitamin C reported so far are too limited to provide conclusive evidence of an effect of vitamin C on blood pressure. In addition, these trials used vitamin C supplementation in very high amounts (>400 mg/d).

Our study has some limitations. Given the cross-sectional design, we cannot infer causality between fruit and vegetable consumption and lower concentrations of LDL-C. However, dietary patterns in adults are relatively stable; and the exclusion of those with prevalent CAD and diabetes mellitus did not alter the results significantly, making it more likely that dietary intakes reported over the past year may reflect the subjects' usual diets. Future studies that use longitudinal data will provide stronger evidence on this association. In addition, frequencies of fruit and vegetable consumption were self-reported; thus, reporting bias might have affected our estimates of the effect. After all, chronic diseases such as CVD are heterogeneous; and along with dietary patterns, other factors such as heredity may need to be considered. Our data indicate that higher intake of fruits and vegetables was associated with lower Keys score and lower percentage of energy from saturated fat. This suggests that residual confounding by saturated fat could have biased our estimates. However, dietary cholesterol did not differ across categories of fruit and vegetable intakes. In addition, the inverse association between fruit and vegetable consumption and LDL-C concentrations was observed across all tertiles of Keys score. Thus, our findings are less likely to be attributable to the effect of substituting saturated fat and dietary cholesterol with fruits and vegetables.

The current study has several strengths including the use of a population-based sample that is representative of Tehran, the use of logistic regression models, and the simultaneous adjustment of confounding variables related to the association between fruit and vegetable consumption and CVD risk factors.

In conclusion, our data show that the consumption of fruits and vegetables is associated with lower concentrations of LDL-C and the risk of CVD per se in a dose-response manner.

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