Published in final edited form as:

Atherosclerosis. 2006 May ; 186(1): 200–206. doi:10.1016/j.atherosclerosis.2005.07.016.

Association between nutrient intake and peripheral artery disease: Results from the InCHIANTI study

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Abstract

Background—Little is known about the relationship between dietary patterns and peripheral arterial disease (PAD). Our aim was to estimate the association between nutrient intake and diagnosis of PAD.

Methods and results—We assessed the nutrient intake of 1251 home-dwelling subjects enrolled in the InCHIANTI study, mean age 68 years (S.D.: 15). We explored the relationship between nutrient intake, obtained through the European Prospective Investigation into Cancer and Nutrition (EPIC) questionnaire, and PAD, defined as an ankle–brachial index (ABI) < 0.90. After adjustment for potential confounders, we found a reduction of the risk of having an ABI < 0.90 associated with vegetable lipid intake ≥ 34.4 g/day (OR: 0.39; 95% CI: 0.16–0.97), Vitamin E intake ≥ 7.726 mg/day (OR: 0.37; 95% CI: 0.16–0.84) and higher serum HDL cholesterol concentration (OR: 0.76; 95% CI: 0.63–0.92 for 10 mg/dl increase). Age (OR: 1.11; 95% CI: 1.07–1.14 for 1 year increase), smoking (OR: 1.03; 95% CI: 1.01–1.04 for 10 packs/year increase) and pulse pressure (OR: 1.11; 95% CI: 1.03–1.19 for 5 mmHg increase) were associated with an increased risk of PAD.

Conclusions—A higher intake of vegetable lipids, Vitamin E and higher concentrations of serum HDL cholesterol characterize subjects free from PAD. Prospective studies are needed to verify whether this dietary pattern and/or interventions aimed at increasing HDL cholesterol exert some protective effect against PAD.

Keywords

Nutrition; Peripheral artery disease; Aging; Epidemiology; Peripheral vascular disease

1. Introduction

Peripheral arterial disease (PAD) is a highly prevalent and prognostically ominous condition [1,2]. Atherosclerotic plaques of the femoral artery have been reported to affect up to two-thirds of subjects aged 56–77 years, and the prevalence increases linearly with age [3]. Smoking, hypercholesterolemia, hypertension, diabetes mellitus and chronic renal failure are well-recognized risk factors for PAD besides age. However, the complex relationships among

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these factors make it difficult to disentangle their respective effects. Furthermore, selected protective factors have been identified; serum HDL cholesterol has been shown to be inversely associated with severity of femoral atherosclerosis both in a large elderly population and in a small population with early onset PAD [3,4]. Also, a low to moderate alcohol intake has been proved to protect from PAD in a longitudinal study [5]. Vitamin C has been hypothesized to have an anti-atherogenic effect based on the association between PAD and subclinical Vitamin C deficiency [6]. Although both antioxidant and anti-inflammatory properties might explain such an effect, the possibility also exists that Vitamin C deficiency is a marker of unhealthy diet or lifestyle instead of being itself a risk factor. Also omega-3 fatty acids, which are effective in both prevention and treatment of coronary artery disease (CAD), have been hypothesized to protect from PAD, but omega-3 fatty acid supplementation failed to improve haemodynamic or clinical outcomes in PAD patients [7]. Finally, the relationship between diet composition and atherosclerosis has been assessed limited to the coronary district, whereas caloric restriction has been reported to be associated with lower carotid artery intima-media thickness [8–10]. It is unknown whether these conclusions apply also to the lower limb vascular district.

These findings suggest that dietary factors should be taken into consideration to define the risk profile for PAD independent of circulating lipids, inflammatory markers and traditional risk factors. The aim of the present study was to verify whether PAD is associated with a distinctive nutritional profile.

2. Methods

2.1. Study population

We used data from the InCHIANTI study, which was designed to investigate the factors contributing to the decline of mobility in older persons [11]. The participants in the study were randomly selected from the populations of two town areas in the Chianti region: Greve in Chianti and Bagno a Ripoli. The Italian National Institute of Research and Care on Aging ethical committee ratified the study protocol. Participants received an extensive description of the study and signed an informed participation consent that included permission to conduct analyses on the biological specimens collected and stored. For those unable to fully consent because of cognitive or physical problems, surrogate consent was also obtained from a close relative. The eligible participants were interviewed at their homes by trained study researcher using a structured questionnaire aimed at investigating their health status, their physical and cognitive performance and other factors possibly related to loss of independence in late life. The interview was followed by a physical examination at the study clinic.

2.2. Definition of lower limb atherosclerosis

We used the Winsor Index (ankle-brachial index, ABI) to identify people affected by PAD. Systolic blood pressure was measured at the right arm and both right and left ankles after a 5 min rest in the supine position, using an ultra-sound probe to detect the first arterial pulse while deflating a standard sphygmomanometer cuff [12]. The ankle-brachial index was obtained by dividing the lower of the two systolic pressures measured at the ankle by the systolic pressure measured at the arm. We considered PAD to be present in people having an ABI < 0.90 [13].

2.3. Assessment of the nutritional intake

The InCHIANTI study included an evaluation of the dietary intake estimated using the questionnaire developed by the European Prospective Investigation into Cancer and Nutrition (EPIC) [14,15]. The EPIC questionnaire is divided into two parts. The first investigates the general dietary pattern and the frequency of meals consumed away from home. The second investigates the intake frequency of 236 specific foods, along with the average size of the serving selected from a range as shown in photographs. The EPIC questionnaire was developed

as a self-administered instrument. However, a preliminary study showed that older persons were prone to misunderstanding some of the questions. Therefore, trained interviewers administered the questionnaire. The information derived from the questionnaire was automatically converted into data on energy, micro- and macronutrient intake, by software specifically designed for the EPIC study. The EPIC nutritional assessment has been successfully validated in the population being studied, by comparing the dietary intake estimated by this method with the dietary intake estimated with a direct method of measure, the weighing and recording of 7-day food consumption [16].

2.4. Assessment of clinical, laboratory and functional data

During the physical examination visit, the study physician collected a detailed clinical history and reviewed the participants' clinical documentation. The diagnosis of hypertension was established using a combination of objective data (blood pressure at examination $\geq 160/90$ mmHg) and anamnestic information (self-report or drug use). The diagnosis of diabetes was made on the basis of fasting serum glucose concentration obtained at the study clinic (glycemia ≥ 140 mg/dl). If the information on serum glycemia was missing, we considered as having diabetes people reporting a diagnosis and taking drugs for diabetes.

For each participant, the InCHIANTI database includes a wide array of laboratory data obtained from blood and urine samples taken while the participant was fasting. Among these are blood and urinary creatinine (from which creatinine clearance was calculated), measured by kinetic colorimetric assay based on modified Jaffé method. The minimum detection limit was 0.1 mg/dl, the interassay coefficient of variation was 2.3% and the intra-assay coefficient of variation was 0.7%. In the attempt to improve the quality of the 24 h urine collection, at the end of the home interview, participants were given precise instructions on the appropriate procedures and asked to annotate possible problems encountered during the collection in an a notebook. Additionally, when the participants handed the container to the investigators, they were asked again about the urine collection. Any mention of a problem invalidated the urine collection and the value was considered missing. Total cholesterol, HDL cholesterol and triglycerides levels were determined by commercial assays (Roche Diagnostics, Mannheim, Germany) and LDL cholesterol calculated using the Friedewald formula. Serum interleukin-1 soluble receptor (IL-1ra) concentration was detected using commercial enzyme-linked immunosorbent assay (ELISA) kits, and serum interleukin-6 (IL-6) concentration was detected using commercial immunoassay kits.

Data regarding physical activity and smoking habits were obtained during the home interview. For physical activity, we used the anamnestic information relative to the third and fourth decade of life if the participant was aged 40 years or less, and relative to the fifth and sixth decade of life for people aged more than 40 years. We decided not to use the information relative to the last year because a low level of physical activity in the last year is likely to be a consequence of PAD and not a risk factor for it.

To quantify the smoking history, we multiplied the mean number of packs of cigarettes smoked daily by the number of years of smoking.

2.5. Analytic strategy

We compared the nutritional profiles of participants with and without PAD. We took into account the intake of different nutrients (available carbohydrates, animal and vegetable proteins, animal and vegetable lipids, fibers, folate, Vitamin C and Vitamin E) that could directly or indirectly be associated with PAD. We analyzed separately the intake of oleic acid, linoleic acid, linolenic acid and of cholesterol. We also considered in the analysis, the total calorie intake and the ratio of the total calorie intake to the ideal body weight, calculated with

the following formula: $(\text{height in cm} - 150) \times 0.8 + \text{age}/2$. We considered as potential confounders socio-demographic factors (age, gender and perceived economic difficulties), smoking (packs/year), physical activity, alcohol intake, serum concentration of total cholesterol, HDL and LDL cholesterol, triacylglycerol, markers of inflammation, such as C-reactive protein, IL-1ra and IL-6, history of diabetes or hypertension, defective renal function (defined as creatinine clearance < 60 ml/min) and blood pressure. In the analysis, the nutrient intake was dichotomized into less than the 75th percentile and equal to the 75th percentile or more. Alcohol intake was categorized as <13 , 13–24 and >24 g/day in men and <7 , 7–12 and >12 g/day in women, because an alcohol intake between 13 and 24 g/day in men and 7–12 g/day in women has been associated with the lower risk of PAD [5]. The association between PAD and nutritional intake was evaluated using contingency tables and calculating the odds ratios along with their 95% confidence intervals. To obtain an estimate of these odds ratios corrected for potential confounders, we used a logistic regression model containing all the variables that were associated with PAD at the crude analysis. Given their established relationship with PAD, we decided to force into the model, the diagnosis of diabetes mellitus and the serum concentration of cholesterol regardless of the association with PAD in this sample. To perform all the analyses we used SAS V8 for Windows (SAS Inc., Cary, NC).

3. Results

Of the initial 1653 participants who were interviewed, we analyzed 1251 persons for whom we had both nutritional and ankle-brachial index information. The mean age was 68.3 years (S.D.: 15.3), and over half of this sample was older than 70 years. Women were 55.3% (692) of the population. The prevalence of PAD was (10%) (125/1251). Table 1 shows the demographic and clinical characteristics of the participants with and without PAD. Participants in the former group were on average 10 years older, less frequently women and had a higher exposure to cigarette smoking. PAD was associated with a lower prevalence of low and moderate levels of physical activity and a higher prevalence of intense levels of physical activity compared to participants without PAD (41.6% versus 30.8% for intense levels of physical activity during the past 20 years). Also, participants with PAD were less frequently moderate alcohol consumers (16.8% versus 29.6%). As expected, participants with PAD had higher concentrations of total serum cholesterol and triacylglycerol and lower concentrations of serum HDL cholesterol. They also had worse renal function and higher concentrations of inflammatory cytokines (IL-1 and IL-6). The prevalence of diabetes mellitus was similar in the two groups (14.2% in the group with PAD versus 9.4% in the group without PAD), while hypertension was more prevalent among those with PAD (47.1% versus 31.2%). In this group, we found higher average systolic blood pressure, but no difference with respect to diastolic blood pressure. This also resulted in a greater pulse pressure in the group with PAD. Average caloric intake was lower among participants with PAD (1904 kcal/day) compared to participants without PAD (2036 kcal/day), and the average calorie/ideal weight ratio was similar between the PAD and non-PAD groups.

Table 2 demonstrates the association between intake selected nutrients and PAD. Carbohydrate, vegetable protein and animal lipid intake were not different between the groups with and without PAD, whereas intake of animal proteins and vegetable lipids were lower in persons with PAD, as compared to those without PAD. In this sample, we found that higher intake of unsaturated fatty acids was associated with less risk of having PAD. This was true for oleic acid (the most common monounsaturated fatty acid in the Italian diet), with an OR of 0.57 (95% CI: 0.35–0.93) as well as for linoleic acid (OR: 0.44; 95% CI: 0.26–0.75), linolenic acid (OR: 0.57; 95% CI: 0.35–0.93) and total polyunsaturated fatty acid (OR: 0.47; 95% CI: 0.28–0.79). Higher intake of vitamins with antioxidant properties was also associated with lower risk of having PAD and this association was most evident for Vitamin E (OR: 0.38; 95% CI: 0.22–0.66).

Table 3 shows the results of a regression model including all factors associated with PAD. When different variables explored the same conceptual parameter (for example, systolic blood pressure and differential blood pressure), we entered in the model the one that we considered more clinically important. In this model, the only nutritional variables associated with PAD were vegetable lipid intake (protective OR: 0.39; 95% CI: 0.16–0.97) and Vitamin E intake (protective OR: 0.37; 95% CI: 0.16–0.84). Other variables associated with PAD were age (OR: 1.11; 95% CI: 1.07–1.14 for 1 year increase), smoking (OR: 1.03; 95% CI: 1.01–1.04 for 10 packs/year increase), serum HDL cholesterol (OR: 0.76; 95% CI: 0.63–0.92 for 10 mg/dl increase) and pulse pressure (OR: 1.11; 95% CI: 1.03–1.19 for 5 mmHg increase). We also tested the interaction between vegetable lipid intake, Vitamin E intake and serum HDL cholesterol by adding interaction terms to the model and found no effect of any of them (data not shown).

4. Discussion

Confirming previous knowledge, in this study, we found that hypertension and smoking are more frequent in patients affected by PAD. High HDL cholesterol and high dietary intake of vegetable lipids and Vitamin E were less frequent in participants with than in those without PAD. Contrary to previous reports, we found no association between alcohol intake and PAD.

We found that higher consumption of vegetable fats was less frequent in patients with than in those without PAD. However, individual fatty acids accounting for such an effect could not be recognized. Interestingly, olive oil was the main source of vegetable fats. Olive oil also provides polyunsaturated fatty acids in an amount up to one-eighth of that of monounsaturated fat [17]. Polyunsaturated fatty acids have been proved to affect favorably both serum lipid profile and endothelial function and to have anticoagulant, anti-inflammatory and anti-aggregant effects [18,19]. However, the relationship between intake and biological activity is unlikely to be linear because many of these effects stem from the interaction of different fatty acids [20]. Furthermore, olive oil contains several molecules, such as flavonoids and terpenes, both of which have antioxidant properties [19]. In the Seven Country study, flavonoid intake was inversely associated with CAD mortality [21]. The negative association between vegetable fat consumption and PAD found in this study might be mediated by molecules different from the fatty acids. This is especially likely in the InCHIANTI study because both the harvesting method and the traditional processing conditions used in Tuscany preserve the antioxidant properties of oil [22,23]. The greater intake of vegetable fats might also be a generic marker of a healthier diet, pointing at a mix of enhanced protective factors and avoidance of “negative” nutrients. The fact that the overall Mediterranean diet but none of its individual components was found to be inversely associated with mortality in the Seven Country study supports this interpretation [24].

Contrary to our findings on PAD, studies on nutritional correlates of CAD allowed to identify both mono- and polyunsaturated fatty acids as protective nutrients. Indeed, the inverse association between intake of monounsaturated fatty acids and coronary risk was confirmed by several observational studies [25]. Both observational and intervention studies claim for a protective role of polyunsaturated fatty acids against CAD [26]. However, in postmenopausal women, intake of monounsaturated acids lacked correlation with angiographically proven progression of CAD, whereas the role of polyunsaturated acid intake changed with the proportion of carbohydrates and non-polyunsaturated fats in the diet [27]. Overall, the identification of select fats as protective against CAD, but not against PAD likely reflects the larger amount of studies made in the former patients. Alternatively, some difference in the dietary modulation of the atherosclerotic process in different vascular districts cannot be excluded. Indeed, omega-3 supplementation lacked any effect on both the pain-free and the maximal distance walked by PAD patients [7], but improved select clinical outcomes in CAD

patients [26]. Finally, the antiarrhythmic effect might partly explain the reported beneficial effect of polyunsaturated acids in CAD patients [28].

A high intake of Vitamin E was negatively associated with PAD. Vitamin E has been shown to have an anti-atherosclerotic effect on the basis of its antioxidant and anti-inflammatory properties, as well as of its inhibitory effect on platelet aggregation and smooth cell proliferation [29]. However, clinical studies failed to show any preventive effect of Vitamin E supplementation on cardiovascular diseases [30]. Furthermore, Vitamin E neither prevents the LDL oxidation induced by non-radical mechanisms nor reduces the oxidative stress in atherosclerotic plaques [31,32]. Thus, the present result might be a chance finding or, more likely, the intake of Vitamin E, as that of vegetable lipids, may be a marker of healthy dietary habits.

The present results do not demonstrate that a low to moderate intake of alcohol protects from atherosclerosis. However, the vasoprotective effect of alcohol has been demonstrated in populations having a lesser intake of olive oil than the InCHIANTI population [5,33]. This might have magnified such an effect. Since an anti-inflammatory effect seems to mediate the vasoprotection afforded by alcohol [33], the inclusion of selected interleukins among potential correlates of ABI might have further concealed the role of alcohol intake in our study. It is worth noting that our results suggest an inverse relationship between higher IL-1ra and ABI, supporting the existence of a link between atherosclerosis and inflammation [34].

The positive association between HDL cholesterol and ABI has been reported by prior studies and may be explained by the protective effect of HDL cholesterol on atherosclerosis progression [3,4,35,36]. Studies have shown that a low HDL cholesterol concentration protects older patients from mortality due to coronary disease and stroke [37], and increasing low HDL cholesterol concentration seems an appropriate target in patients with or at risk for PAD. However, cardiac and cerebrovascular mortality and morbidity, but not the onset or progression of PAD, were the outcomes of statin-based intervention trials, as well as of the few trials combining statins with niacin, which is the most effective agent available for increasing HDL cholesterol [38,39].

Systolic hypertension, but not a diagnosis of hypertension, was an independent correlate of PAD. This finding is not surprising, because the variable quality of the antihypertensive therapy is likely to affect the relationship between hypertension and atherosclerosis. Furthermore, systolic hypertension has been reported to overcome diastolic hypertension as a negative prognostic marker of cardiovascular mortality and morbidity in the elderly [40]. Finally, systolic hypertension is a direct measure of the vessel wall rigidity, thus reflecting the severity of atherosclerosis [41].

Limitations of this study require comments. First, to calculate the ABI, we used the blood pressure measured at the right arm only, instead of the higher brachial pressure of the right and left arms. Since there is an equal probability of finding higher pressure in either side, this non-differential misclassification would lead to a dilution of the associations observed. Second, even the most sophisticated statistical analysis cannot completely separate the respective effect of the many recognized and hypothetical atherogenic factors. For example, we cannot rule out the possibility that a high intake of vegetable fatty acids was not protective per se but was rather a marker of a higher intake of plant sterols and other nutrients having a well-known hypocholesterolemic effect [42]. Third, some of the assessed correlates of PAD, such as high systolic arterial pressure, were both potential causes and to some extent effect of atherosclerosis. Fourth, the lack of patients with clinically moderate to severe PAD prevented us from assessing the full spectrum of the correlation between putative causal factors and abnormal ABI. This might have weakened some associations, therefore, hampering a full-scale

definition of the relative weights of individual risk factors. Finally, given the cross-sectional nature of this study, we can only describe associations, but not prove causal relationships.

In conclusion, our findings suggest that persons with a high intake of vegetable lipids, mainly of olive oil and Vitamin E are less likely to be affected by PAD. If confirmed in prospective studies, the possibility that both dietary interventions and strategies to increase HDL cholesterol might be valuable for preventing or slowing down the clinical progression of PAD should be investigated in intervention studies.

Acknowledgements

The InCHIANTI project was supported as a targeted project by the Italian Ministry of Health (ICS110.1/R597.71).

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Table 1
Demographic and clinical characteristics of participants

	Participants without PAD (<i>n</i> = 1126)	Participants with PAD (<i>n</i> = 125)	<i>P</i>
Age (S.D.)	67.1 (15.6)	78.5 (7.6)	<0.001
Gender (% women)	56.9%	40.8%	<0.001
Perceived economic difficulties	8.0%	10.5%	0.362
Smoking (packs/year)	9.6 (16.8)	22.7 (25.5)	<0.001
Physical activity			
Sedentary/light	24.1%	20.8%	0.047
Moderate	45.1%	37.6%	
Intense	30.8%	41.6%	
Alcohol intake			
<13 g/day (M) or 7 g/day (W)	14.8%	16.0%	0.010
13–24 g/day (M) or 7–12 g/day (W)	29.6%	16.8%	
>24 g/day (M) or >12 g/day (W)	55.6%	67.2%	
Total cholesterol (mg/dl) (mean ± S.D.)	215.1 ± 39.9	221.8 ± 40.8	0.082
HDL cholesterol (mg/dl) (mean ± S.D.)	56.6 ± 14.8	50.3 ± 14.3	<0.001
Triacylglycerol (mg/dl) (mean ± S.D.)	122.6 ± 76.2	151.6 ± 74.1	<0.001
C-reactive protein (mg/dl) (mean ± S.D.)	0.8 ± 2.5	0.9 ± 1.2	0.424
Creatinine (mg/dl) (mean ± S.D.)	0.91 ± 0.2	1.03 ± 0.4	0.002
Creatinine clearance (mean ± S.D.)	84.3 ± 30.3	68.3 ± 28.2	<0.001
IL-6 (pg/ml) (mean ± S.D.)	1.8 ± 3.1	3.6 ± 8.2	0.019
IL-1RA (pg/ml) (mean ± S.D.)	151.9 ± 115.4	190.7 ± 176.1	0.018
Diabetes mellitus (%)	9.4%	14.2%	0.106
Hypertension (%)	31.2%	47.1%	<0.001
Systolic blood pressure (mmHg) (mean ± S.D.)	144.6 ± 21.3	155.0 ± 19.6	<0.001
Diastolic blood pressure (mmHg) (mean ± S.D.)	82.7 ± 9.3	71.2 ± 15.0	0.224
Differential blood pressure (mean ± S.D.)	61.9 ± 15.9	71.2 ± 15.0	<0.001
Total calories intake (kcal) (mean ± S.D.)	2036.9 ± 632	1904.6 ± 490	0.007
Calories/ideal weight ratio (mean ± S.D.)	25.2 ± 8.1	22.5 ± 6.0	<0.001

Table 2Prevalence of nutrient intake ≥ 75 th percentile

	Participants without PAD (<i>n</i> = 1126) (%)	Participants with PAD (<i>n</i> = 125) (%)	OR (95% CI)	<i>P</i>
Carbohydrate intake ≥ 303 g/day	25.6	20.3	0.74 (0.47–1.17)	0.196
Animal protein intake ≥ 59 g/day	26.1	17.9	0.62 (0.38–0.99)	0.047
Vegetable protein intake ≥ 34 g/day	25.8	21.1	0.77 (0.49–1.22)	0.265
Animal lipid intake ≥ 43 g/day	25.7	19.5	0.70 (0.44–1.11)	0.131
Vegetable lipid intake ≥ 41 g/day	26.7	14.6	0.47 (0.28–0.79)	0.003
Fiber intake ≥ 23.5 g/day	26.5	18.7	0.64 (0.40–1.03)	0.062
Oleic acid intake ≥ 39.0 g/day	26.5	17.1	0.57 (0.35–0.93)	0.022
Linoleic acid intake ≥ 7.0 g/day	26.6	13.8	0.44 (0.26–0.75)	0.002
Linolenic acid intake ≥ 1.2 g/day	26.5	17.1	0.57 (0.35–0.93)	0.023
Polyunsaturated fatty acids intake ≥ 8.8 g/day	26.5	14.6	0.47 (0.28–0.79)	0.004
Folate intake ≥ 316.1 mcg/day	26.4	17.1	0.57 (0.35–0.94)	0.025
Vitamin C intake ≥ 144.1 mg/day	26.2	17.9	0.61 (0.38–0.99)	0.045
Vitamin E intake ≥ 7.7 mg/day	26.8	12.2	0.38 (0.22–0.66)	<0.001

Table 3

Multivariable logistic regression modeling the probability of having PAD

	OR	95% CI
Age	1.11	1.07–1.15
Gender (men)	1.01	0.55–1.84
Smoking (10 packs/year)	1.03	1.02–1.04
Physical activity		
Sedentary/low	1	—
Moderate	0.87	0.47–1.59
Intense	1.06	0.56–1.99
Alcohol intake		
13–24 g/day (M) or 7–12 g/day (W)	1	—
<13 g/day (M) or <7 g/day (W)	0.67	0.32–1.40
>24 g/day (M) or >12 g/day (W)	0.81	0.44–1.48
Diabetes mellitus	0.81	0.40–1.63
Serum HDL cholesterol (10 mg/dl increase)	0.76	0.62–0.92
Serum triacylglycerol (10 mg/dl increase)	1.01	0.98–1.04
IL-6 (10 pg/ml increase)	1.04	0.56–1.94
IL-1ra (10 pg/ml increase)	1.01	0.99–1.03
Creatinine clearance < 60 ml/min	1.16	0.67–2.00
Differential blood pressure (5 mmHg increase)	1.10	1.02–1.18
Calories intake/ideal weight ratio	1.0	0.94–1.06
Fiber intake (highest quartile)	0.85	0.42–1.70
Animal protein intake (highest quartile)	0.68	0.35–1.34
Vegetable lipid intake (highest quartile)	0.30	0.11–0.79
Oleic acid intake (highest quartile)	1.84	0.66–5.14
Total PUFA intake (highest quartile)	1.20	1.01–1.43
Folate acid intake (highest quartile)	0.94	0.42–2.13
Vitamin C intake (highest quartile)	1.29	0.62–2.69
Vitamin E intake (highest quartile)	0.39	0.16–0.92