Association Between Diet, Lifestyle, Metabolic Cardiovascular Risk Factors, and Plasma C-Reactive Protein Levels

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Increased C-reactive protein (CRP) levels have been associated with several of the components of the metabolic syndrome, but the direct influence of diet and lifestyle factors on CRP levels remains largely unknown. The purpose of the present study was to investigate the association between CRP and diet and lifestyle factors. Plasma CRP levels were determined by a highly sensitive enzyme-linked immunosorbent assay (ELISA) in 760 participants in the β-Blocker Cholesterol-Lowering Asymptomatic Plaque Study (BCAPS). In accordance with previous findings, increased levels of CRP were associated with high body mass index (BMI) ($P = .012$), triglycerides ($P = .001$), systolic blood pressure ($P = .019$), cholesterol/high-density lipoprotein (HDL) ratio ($P = .009$), and low HDL cholesterol ($P = .001$). CRP was also increased in smokers ($P = .023$) and in subjects with a low vitamin C intake ($P = .018$). When men and women were analyzed together, there were no significant associations between CRP and dietary intake of total calories, total fat, saturated fat, monounsaturated fat, polyunsaturated fat, n-3 polyunsaturated fatty acids, n-6 polyunsaturated fatty acids, fiber, vitamin E, carotene, or selen, or in physical activity. However, in the female subgroup weak inverse relations were observed between CRP and the intake of total fat ($r = -0.13$, $P = .011$), saturated fat ($r = -0.13$, $P = .011$), monounsaturated fat ($r = -0.13$, $P = .010$), polyunsaturated fat ($r = -0.14$, $P = .007$), and n-3 PUFA ($r = -0.14$, $P = .004$). Stratified factor analyses in smoking subgroups, obese, and in under-reporters of energy, largely confirmed the results although in male never-smokers a combination of high fiber vitamin C/beta carotene intake was associated with low CRP levels. These observations suggest that CRP levels are only marginally associated with individual dietary and lifestyle factors. Surprisingly, a higher intake of fat tended to be associated with lower CRP values among women.

DURING RECENT YEARS a convincing body of evidence has established C-reactive protein (CRP) as a strong independent risk factor for cardiovascular disease.[1] Elevated levels of CRP in apparently healthy men and women have been associated with an increased risk for development of coronary heart disease, stroke, and peripheral vascular disease.[2-6] CRP has also been demonstrated to be significantly associated with the severity of coronary plaques and carotid intima-media thickness (IMT).[7,8]

The biologic mechanisms responsible for the association between CRP and cardiovascular disease remain to be fully understood. CRP is an inflammatory marker synthesized primarily by hepatocytes in response to interleukin (IL)-6, IL-1, tumor necrosis factor α (TNFα), and other cytokines.[9] The findings that CRP is present in atherosclerotic plaques, binds to low-density lipoprotein (LDL) promoting its uptake in macrophages, and activates the complement system, as well as tissue factor, suggest that CRP may actively contribute to the development of cardiovascular disease.[10,11] It is also possible that increased CRP levels are a marker of the inflammatory activity in atherosclerotic lesions throughout the arterial system. The latter possibility is supported by the observations that increased levels of several other inflammatory markers, such as IL-6, vascular cell adhesion molecule-1 (VCAM-1), and intercellular adhesion molecule-1 (ICAM-1), also are associated with increased risk for development of cardiovascular disease.[5,12,13]

Irrespective of whether CRP acts directly on the artery wall or is a marker of arterial inflammation, it is important to reach a better understanding of the factors associated with increasing CRP levels. Previous studies have demonstrated that age, smoking, body mass index (BMI), fasting glucose, insulin sensitivity, plasma triglycerides, and low high-density lipoprotein (HDL) cholesterol are associated with increased CRP levels.[14-18] However, it remains to be established whether the increase in CRP is the result of metabolic changes associated with the metabolic syndrome or if it is induced by any of the individual dietary and lifestyle factors known to be involved in the development of the metabolic syndrome. The aim of this study was to test the hypothesis that differences in CRP levels are associated with particular dietary habits and lifestyle factors.

METHODS

Study Population

The background population for this study consisted of all men and women born between 1926 and 1945 and living in Malmö, Sweden (n = 68,905 in 1991). The population was identified by use of the Swedish National Population registries. Probands were invited by mail and by advertising to take part in the Malmö Diet and Cancer Study (MDCS).[19] The participation rate was 39% (n = 28,098) and the participants were shown to have a lower mortality than nonparticipants.[20] The MDCS has a cardiovascular component randomly chosen from the participants in the MDCS[21] in which the degree of atherosclerosis was determined by B-mode ultrasound.

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Table 1. Baseline Clinical Characteristics

Age (yr)	61.3 ± 5.4
Male sex (%)	45.5
Former smokers (%)	36.9
Current smokers (%)	30.8
BMI (kg/m^2)	25.5 ± 3.6
Waist-hip ratio	0.85 ± 0.09
Waist circumference (cm)	83.1 ± 11.9
Systolic blood pressure (mm Hg)	138.9 ± 14.4
Diastolic blood pressure (mm Hg)	84.7 ± 7.1
Glucose (mmol/L)	5.1 ± 0.7
Total cholesterol (mmol/L)	6.12 ± 0.98
LDL cholesterol (mmol/L)	4.14 ± 0.88
HDL cholesterol (mmol/L)	1.38 ± 0.37
Total cholesterol/HDL cholesterol	4.70 ± 1.29
Triglycerides (mmol/L)	1.3 ± 0.64

The study group for the present analyses consisted of 760 men and women, 49 to 70 years of age, with a plaque in the right carotid artery but no symptoms of carotid artery disease participating in the β-Blocker Cholesterol-Lowering Asymptomatic Plaque Study (BCAPS) trial,[21] which recruited subjects from the MDCS participants. The study group did not include subjects regularly using β-blockers or statins, or those with systolic blood pressure above 160 mm Hg, diastolic blood pressure above 95 mm Hg, total cholesterol greater than 8.0 mmol/L, or hyperglycemia suspected to require insulin treatment. The baseline characteristics of the study group are presented in Table 1. A history of cardiovascular disease was present in 4.3% of the subjects and 3.2% had a history of type 2 diabetes. Forty-two percent of the women received hormone-replacement therapy. The study was approved by the ethics committee and all procedures followed the Declaration of Helsinki.

Data Collection

Study subjects visited the MDCS center twice. At the first visit, project staff provided information on the background and aim of the study and detailed information on lifestyle and dietary data collection procedures. At the second visit, 2 weeks later, the subjects were assigned to interviewers who helped each subject to complete the diet history and check the lifestyle questionnaire. An ultrasound examination of the right carotid artery was performed. Subjects with a plaque in the right carotid artery were invited to take part in BCAPS, a randomized, double-blind study comparing the effect of metoprolol CR/XL, fluvastatin, and placebo on the degree of atherosclerosis during 3 years of treatment.[21] Blood for determination of CRP and biochemical cardiovascular risk factors were collected between 8 AM and 10 AM after overnight fasting at the BCAPS baseline visit. The interval between the last dietary interview and blood sampling was 6 to 8 months.

Dietary Assessment

The MDCS diet assessment method has been described previously[22] and the reproducibility and validity have been published.[23,24] In brief, it is a modified diet history method combining a menu book for cooked meals and a 168-item food frequency questionnaire on regularly consumed foods during the last year. Low energy reporting is a major concern in dietary assessment.[25] The ratio between reported total energy intake (EI) and Basal Metabolic Rate (BMR) was calculated. BMR was calculated using an equation based on age, sex, weight, and height (World Health Organization Technical Reports Series, WHO, Geneva, 1985). At group level a ratio below 1.35 was used as an indicator of under-reporting energy.[26]

Definition of Alcohol Consumption, Physical Activity, and Educational Level

Alcohol intake was assessed from the 7-days menu book registration.[24] Alcohol consumption is defined into 4 groups according to an assumption of biologic risk (none = subjects who did not reported any alcohol consumption in the menu book and no alcohol consumed during the last 30 days; low = <20 g [men] and <15 g [women] alcohol per day; medium = 20 to 40 g [men] and 15 to 30 g [women] alcohol per day; and high = >40 g [men] and >30 g [women] alcohol per day).

Physical activity during leisure time was assessed by a list of 18 different activities in the questionnaire, adapted from the Minnesota Leisure Time Physical Activity Questionnaire.[27] A physical activity score was obtained by computing the sum of all activity products reported in the questionnaire. Four categories (ie, low, mild, moderate, and high) of physical activity status were identified by the subjects' quartile ranking.

Information on education and occupation was obtained from a self-administered questionnaire. Educational level was classified into three categories. Primary education included those who had less than 9 years of education, some secondary education included those who had 9 to 11 years of education, and completed secondary education included those who had completed secondary school (12 years) and those who had education at the college or university level.

Risk Factors for Cardiovascular Disease

Blood pressure was measured in the supine position after 5 minutes rest with a mercury manometer attached to a rubber cuff of appropriate sizes for the arm circumference by 2 experienced nurses at the BCAPS baseline visit. Smoking habits were classified as current smokers, ex-smokers or never-smokers.

Total plasma and HDL cholesterol and triglycerides were measured from blood collected after an overnights fast, with the routine clinical methods used at the Department of Clinical Chemistry, Malmö University Hospital. LDL cholesterol levels were calculated according to Friedewald equation.

CRP Analysis

CRP was analyzed in plasma samples gathered at the baseline examination (second visit) for the BCAP study, using a highly sensitive method developed in the Department of Medicine at the Malmö University Hospital at Lund University. Plasma CRP was measured with the use of a rabbit anti-human CRP (A0073, Dako A/S, Glostrup, Denmark) as capture antibody, rabbit anti-human CRP (P0227 peroxidase-conjugated, Dako) for detection, human CRP high control (X0926, Dako) as standard, and TMB One-Step Substrate (S1600, Dako) as substrate.[28] The detection limit was 0.1 μg/L (intercoefficient of variation = 8%).

Statistical Analysis

Differences between groups were tested by *t* test and chi-square test, as applicable. Daily average nutrient intakes with supplements were calculated. Most variables had positively skewed distributions and were hence log-transformed before statistical tests.

Values for metabolic variables, dietary data, and lifestyle factors were divided into quartiles and the mean CRP level determined for each quartile. Analyses of covariance were used for trend analysis with the logarithm of CRP as the dependent variable and quartiles of risk factors and diet variables as independent variables adjusted for age and sex.

Factor analysis was used to examine the inter-relationship among the independent variables, split by gender and smoking habits. Factor rotations were done with the varimax method. Factors with eigen

Table 2. Association Between Metabolic Cardiovascular Risk Factors and Plasma CRP Levels

	Q1	Q2	Q3	Q4	*P* for Trend
BMI (kg/m^2)	1.80	2.01	2.28	2.59	.012
Waist-hip ratio	2.05	2.11	2.23	2.30	.105
Waist circumference	2.25	2.12	2.05	2.26	.96
Diastolic blood pressure	2.19	2.01	2.01	2.64	.106
Systolic blood pressure	1.73	2.16	2.48	2.58	.019
Cholesterol	2.31	2.16	2.03	2.16	.563
LDL	2.19	2.17	2.31	1.99	.439
HDL	2.71	2.34	2.10	1.54	.001
Cholesterol/HDL	1.70	2.11	2.32	2.54	.009
Triglycerides	1.80	2.01	2.27	2.58	.001
Glucose	1.84	2.17	2.18	2.60	.112

NOTE. CRP levels are in mg/L. Values for cardiovascular risk factors were divided into quartiles.

values greater than 1.0 were correlated with the logarithm of CRP. Factors with loading scores above 0.5 were considered as contributing factors. In the factor analyses, subjects were stratified into current, former, and never-smokers, into subjects with BMI = 25 or >25 kg/m^2, and into subjects with EI/BMR <1.35 or ≥1.35.

RESULTS

CRP and Cardiovascular Risk Factors

There was no difference in CRP between women receiving hormone-replacement therapy (2.20 ± 2.20 mg/L) and those who did not (1.99 ± 2.30 mg/L). Subjects with a history of type 2 diabetes had higher plasma levels of CRP (2.72 ± 2.69 mg/L *v* 2.11 ± 2.33 mg/L, $P = .005$), but no significant difference was detected in subjects with or without a history of cardiovascular diseases (1.67 ± 1.36 mg/L *v* 2.19 ± 2.41 mg/L). CRP was found to increase with BMI, with plasma levels being 40% higher in those with a BMI above 27.6 kg/m^2 than those with a BMI below 23.1 kg/m^2 (Table 2). A similar difference in CRP levels was also observed between the highest and lowest quartiles of triglycerides and systolic blood pressure. The latter was not affected by adjusting for antihypertensive treatment. There was a strong inverse association between HDL cholesterol and CRP, with CRP levels being 88% higher in subjects with a HDL cholesterol below 1.1 mmol/L than in those with an HDL cholesterol above 1.6 mmol/L. Moreover, a high total cholesterol/HDL cholesterol level was also associated with increased CRP levels. CRP also tended to increase with increasing fasting glucose levels, but there was no relationship between CRP and total cholesterol or LDL cholesterol (Table 2).

There was a 40% difference between smokers and nonsmokers ($P = .005$, *t* test). Using an analysis of variance for differences between nonsmokers, former smokers, and present smokers, the *P* value for trend was .023 (Fig 1A). However, there was no difference in individuals smoking less than 10 g/d of tobacco and those smoking 11 g/d or more (2.66 mg/L *v* 2.49 mg/L). No significant associations were found between CRP and alcohol consumption (Fig 1B) or physical activity (Fig 1C). CRP levels were lower among those that completed at least 12 years of education (Fig 1D).

CRP and Dietary Factors

Univariate analyses. When men and women were analyzed together, there were no statistically significant associations between CRP and dietary intake of total calories, total fat, fat intake adjusted for calorie intake, saturated fat, monounsaturated fat, polyunsaturated fat, the polyunsaturated/staturated fat (P/S) ratio, omega-3 fatty acids, and omega-6 fatty acids. There was a weak but nonsignificant inverse association between CRP and the dietary intake of fiber (Table 3). A low intake of vitamin C was associated with increased CRP levels. A similar but nonsignificant trend was seen also for CRP and the intake of vitamin E (Table 3). There was a weak inverse association between total intake of carbohydrates and CRP ($r = -0.07$,

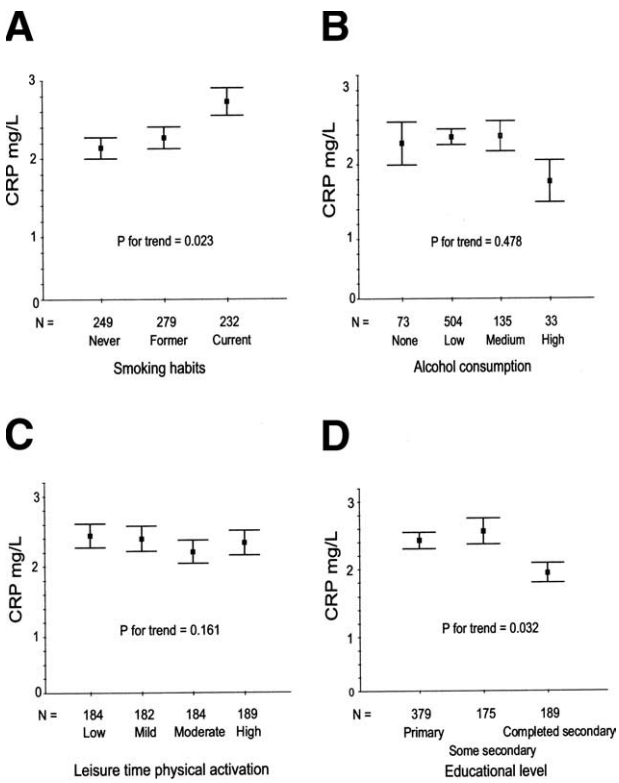

Fig 1. Baseline mean (± SE) sensitive CRP concentration in men and women participating in the BCAPS defined into groups by smoking habits (A), alcohol consumption (B), leisure time physical activity (C), and educational level (D).

Table 3. Association Between Diet and Plasma CRP Levels

	Q1	Q2	Q3	Q4	*P* for Trend
Total calories	2.39	2.20	2.10	1.86	.12
Total fat	2.18	2.39	2.01	1.98	.33
Total fat/energy	1.99	2.33	2.04	2.19	.81
Vitamin C	2.73	1.95	2.23	2.10	.02
Vitamin E	2.33	2.23	2.10	1.93	.14
Carotene	2.33	2.17	2.16	1.88	.34
Selen	2.00	2.26	2.10	2.18	.85
Saturated fat	2.38	2.13	2.10	1.94	.16
Monounsaturated fat	2.34	2.22	1.94	2.05	.24
Polyunsaturated fat	2.23	2.11	2.31	1.81	.25
P/S ratio	2.19	2.22	1.96	2.18	.91
n-3 PUFA	2.25	2.28	2.01	2.00	.10
n-6 PUFA	2.24	2.00	2.51	1.79	.81
Fiber	2.50	2.25	2.05	1.77	.12
Fiber/energy	2.47	2.24	2.05	1.80	.25

NOTE. CRP levels are in mg/L. Values for dietary variables were divided into quartiles.
Abbreviation: PUFA, polyunsaturated fatty acids..

$P < .05$), whereas there were no relationships between CRP and total intake of calcium, protein, and sugar. Similar trends were observed when men and women were analyzed separately. However, among women weak but statistically significant inverse relations were observed between CRP and the intake of total fat ($r = -0.13$, $P = .011$), saturated fat ($r = -0.13$, $P = .011$), monounsaturated fat ($r = -0.13$, $P = .010$), polyunsaturated fat ($r = -0.14$, $P = .007$), and n-3 polyunsaturated fatty acids ($r = -0.14$, $P = 0.004$).

Multivariate analyses. Separate analyses of the association between total fat intake and CRP with concomitant adjustment for energy intake or the other subtype of fat intake did not change the results from the above univariate analyses.

Importance of Smoking, Obesity, and Under-reporting

Effects of these possible confounders were analyzed by stratified factor analyses. The analyses were repeated separately for current smokers, ex-smokers, and never-smokers, subjects with BMI above and below 25 kg/m^2, and for under-reporters, ie, an EI/BMR ratio below 1.35.

Smoking. The factor analysis yielded similar factors for current smokers, never-smokers, and former smokers (Table 4). The degree of physical activity did not influence CRP levels in any of the groups. For female current smokers 3 factors emerged accounting for 72% of the total variance. The first component was characterized by high total fat intake, saturated and monounsaturated fat intake, and high EI. The second component incorporated high intake of fiber, vitamin C, and beta-carotene, while the third component included age of participant and BMI. For male current smokers 4 components explained 78% of the variation, with a similar first component. Component 2 was characterized by high intake of polyunsaturated fat and vitamin E, while components 3 and 4 were similar to component 2 and 3 among the women. These associations did not change if men and women were grouped according to waist circumference (using 90 cm as cut-off for men and 80 cm for women) instead of BMI.

Correlation coefficients between the high-loading components and CRP concentrations at baseline were calculated. Only 2 components were significantly related to CRP. In male never-smokers component 3 (intake of fiber, vitamin C, and beta-carotene) was negatively correlated ($r = -0.44$, $P < .0001$) with CRP. In female former smokers component 1 (high intake of fat and energy) was negatively correlated ($r = -0.21$, $P < .02$) with CRP.

Similar analyses were performed for subjects with BMI above or below 25 kg/m^2 and subjects suspected to under-report energy, ie, EI/BMR below 1.35. For lean males (BMI $<$ 25 kg/m^2) 4 components with eigen values above 1 explained 76% of the variance. The components were equal to these mentioned above. Only one factor explaining approximately 9% of the variance was significantly and negatively associated with CRP ($r = -0.26$, $P < .001$). This component was the high fiber/vitamin C/beta-carotene component.

Also in the EI/BMR analyses the components and the degree of explained variance were similar. For both men and women with EI/BMR <1.35, the fourth component explaining 7% of the variance and composed of older subjects with high BMI, was significantly correlated to CRP ($r = 0.23$ for both sexes, $P = .04$ for men and .014 for women). For men with EI/BMR ≥ 1.35, the third component (fiber, vitamin C, and beta-carotene) explaining 9% of the variance was significantly negatively associated with CRP ($r = -0.23$, $P < .001$).

DISCUSSION

Low-grade inflammation as assessed by moderately increased CRP levels is a strong independent risk factor for development of cardiovascular events.[29] To prevent the development of cardiovascular disease in individuals with elevated CRP levels it is important to reach a better understanding of the factors that cause this phenomenon. Several studies have demonstrated that obesity, type 2 diabetes and presence of a metabolic syndrome are associated with increased plasma levels of CRP.[14-18] Significant associations exist between CRP and individual components of the metabolic syndrome such as a high BMI, abdominal obesity, hypertension, hypertriglyceridemia,

Table 4. Stratified Factor Analyses in Current, Former, and Never-Smokers in Subjects With BMI = 25 or >25 kg/m^2

Group	Eigen-Value	% of Variance	Cummulative %	Component Characteristics (related component matrix)
Men				
Smoking				
Current				
Component 1	6.5	46	46	High fat and energy intake
2	2.0	14	61	High PUFA and vitamin E
3	1.4	10	71	High fiber, vitamin C, β-carotene
4	1.0	7	78	Age
Former				
Component 1	6.8	49	49	See component 1 current
2	1.7	12	60	See component 3 current
3	1.2	8	69	High BMI
4	1.0	7	76	See component 4 current
Never				
Component 1	6.1	44	44	See component 1 current
2	2.0	14	58	See component 2 current
3	1.4	10	68	See component 3 current
4	1.2	8	77	High BMI and Se intake
Women				
Smoking				
Current				
Component 1	6.8	49	49	High fat and energy intake
2	2.1	15	64	High fiber, vitamin C, β-carotene
3	1.1	8	72	High BMI
Former				
Component 1	6.6	47	47	See component 1 current
2	2.1	15	62	See component 2 current
3	1.2	8	71	High age, BMI and Se intake
Never				
Component 1	6.3	45	45	See component 1 current
2	2.2	16	61	See component 2 current
3	1.1	8	69	See component 3 current

and low HDL cholesterol.[14-18,30] However, it has not been clarified whether the increase in CRP occurs in response to any particular dietary or lifestyle factors associated with development of the metabolic syndrome.

Significant associations between elevated CRP and a high BMI, a high systolic blood pressure, high triglycerides, and low HDL cholesterol were observed in the present study population, confirming several previous studies demonstrating increased CRP levels in individuals with one or more components of the metabolic syndrome.[14-18,31,32] However, there were no significant associations between CRP and total intake of fat or calories. Moreover, no significant associations were found between CRP and the intake of saturated, monounsaturated or polyunsaturated fat, as well as intake of omega-3 or omega-6 fatty acids. There was also no association between CRP levels and the degree of physical activity. The latter observation is in contrast to several previous studies.[33,34] The reason for this discrepancy remains unclear but one possibility is that our physical questionnaire was not sensitive enough in this respect. When the influence of smoking, overweight, and under-reporting was determined in stratified factor analyses, the only component that seemed to be associated with a low CRP, was a component characterized by high intake of fiber, vitamin C, and beta-carotene, a pattern consistent with a healthy diet. These observations suggest that the elevation in CRP is caused by the factors associated with a metabolic syndrome rather than by any of the individual dietary or lifestyle factors known to be associated with this syndrome.

Several components of the metabolic syndrome have potentially proinflammatory effects. Triglyceride-rich lipoproteins, such as very-low-density lipoprotein (VLDL), stimulate activation of the proinflammatory transcription factor NF-κB, as well as the expression of TNFα, ICAM-1, and VCAM-1 in the arterial endothelium in vivo.[35] VLDL stimulates the release of plasminogen activator inhibitor-1 (PAI-1), another component of the metabolic syndrome, in endothelial cells by activating binding of a transcription factor to a VLDL-responsive promoter-site in endothelial cells.[36] Hypertriglyceridemia is associated with formation of small dense LDL particles that more easily penetrate the arterial wall and become oxidized, potentially resulting in vascular damage and inflammation.[37] HDL has been shown to have anti-inflammatory properties and low HDL levels may thus further contribute to the establishment of vascular inflammation.[38] Finally, advanced glycemic modification of lipoproteins, as well as other proteins, in response to hyperglycemia may also cause to the activation of inflammation.[39]

The influence of dietary fat intake on CRP remains largely unknown. Using a low-sensitive CRP assay, Ernst et al[40] found no effect on CRP levels by a 1 g/d intake of n-3 polyunsatu-

rated fatty acids for 3 weeks. Madsen et al[7] have reported an association between docosahexoenic acid (22:6 n-3) levels in granulocyte membranes and CRP levels, while no associations were found between n-6 polyunsaturated fatty acids levels in granulocyte membranes and CRP. Experimental studies have provided some support for an anti-inflammatory role of n-3 polyunsaturated fatty acids, including an inhibition of cytokine release from endothelial cells,[41,42] while the experimental data suggest that n-6 polyunsaturated fatty acids (mainly linoleic acid and arachidonic acid) may have proinflammatory effects.[43] The association between a high intake of n-3 polyunsaturated fatty acids and low CRP observed in the present study support the notion that n-3 polyunsaturated fatty acids may have a beneficial effect on low-grade inflammation. The mechanism responsible for the weak, but statistically significant, inverse association between CRP and total intake of fat, saturated fat, monounsaturated fat and polyunsaturated fat among women remains to be fully understood.

Several studies have suggested that antioxidant vitamins influence CRP expression. Langlois et al[44] have reported that patients with peripheral artery disease have decreased levels of vitamin C and that there is a strong inverse relation between the plasma levels of vitamin C and CRP in these patients. Accordingly, a low intake of vitamin C was found to be associated with increased CRP in the present study. Vitamin E supplementation (1,200 IU/d) for 3 months has been shown to reduce CRP levels in both healthy controls and patients with type 2 diabetes by more than 50%.[45] Inverse associations between CRP and beta-carotene have been found when examining the 14,470 participants in the National Health and Nutrition Examination Survey.[46] However, while many epidemiologic studies have suggested a protective role of antioxidant vitamins in cardiovascular disease, most of the randomized antioxidant intervention trials have failed to confirm this effect.

Recent data from Liu et al[47] in a study on 244 apparently healthy women suggest that intake of rapidly digested and absorbed carbohydrates with a high dietary glycemic load is associated with increased CRP levels. In accordance, there was a nonsignificant inverse trend between CRP and the dietary intake of fiber in the present study. Previous studies from our group have also provided evidence suggesting that a fiber-rich diet reduces the risk for development of a metabolic syndrome.[48]

There are limitations to the present study. First, the study population may not have been large enough to identify minor associations between CRP and some dietary constituents. Second, there was a lag phase of 6 to 8 months between obtaining the dietary data and the blood sampling for CRP analysis. However, validation studies have demonstrated that the dietary data obtained by this method are reasonably stable over a long period of time.[23,24] Third, many statistical analyses were performed and the risk of mass significances must be taken into account.

In summary, the present study suggest that CRP levels become elevated in response to the factors that are associated with a metabolic syndrome rather than by any particular dietary constituent. Smoking appears to be another important factor contributing to increased plasma CRP levels.

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