Circulation primary angioplasty for acute myocardial infarction: myocardial blush grade.

F. Angiographic assessment of myocardial reperfusion in patients treated with device during percutaneous intervention in saphenous vein aorto-coronary bypass

Popma JJ, Ho KKL, Kuntz RE. A randomized trial of a distal embolic protection

Briguori C, Dharmadhikari A, Sheiban I, Colombo A. Prevention of distal

patients with acute myocardial infarction.


Relation of Dietary Fat and Fiber to Elevation of C-Reactive Protein

Dana E. King, MD, Brent M. Egan, MD, and Mark E. Geesey, MS

We examined the relation of dietary fiber, fat, and other dietary factors to levels of highly sensitive C-reactive protein (CRP) in 4,900 adult participants in the 1999 to 2000 National Health and Nutrition Examination Survey (NHANES 99-00), which was a cross-sectional study of a nationally representative sample of noninstitutionalized United States residents. After controlling for demographic factors, body mass index, smoking, alcohol consumption, exercise, and total caloric intake, subjects in the third and fourth highest quartiles of fiber consumption had a lower risk of elevated CRP (odds ratio [OR] 0.64, 95% confidence interval [CI] 0.43 to 0.96; OR 0.58, 95% CI 0.38 to 0.88, respectively) compared with the lowest quartile. Saturated fat consumption was modestly associated with elevated CRP (third quartile: OR 1.58, 95% CI 1.02 to 2.44; fourth quartile 1.44, 95% CI 0.80 to 2.58). The findings suggest that inflammation may link dietary fiber and fat to cardiovascular disease. ©2003 by Excerpta Medica, Inc.

(Am J Cardiol 2003;92:1335–1339)

To investigate the relation between specific dietary factors and C-reactive protein (CRP), we conducted a study using the 1999 to 2000 National Health and Nutrition Examination Survey (NHANES 99-00), a national study of the civilian, noninstitutionalized population in the United States. Use of this database offers several advantages, including a national sample, availability of highly sensitive CRP assays, and the ability to control for possible confounders in the relation, including race, obesity, and smoking. The purpose of the present study was to determine whether consumption of specific food components is associated with elevation of CRP. This information could have important implications for biologic mechanisms linking diet and heart disease and could also serve to help refine and strengthen dietary guidelines for the population.

We derived our study sample from the participants in the NHANES 99-00. The NHANES 99-00 is the most recent release of this nationally representative, complex, multistage, probability-based survey of the civilian, noninstitutionalized population of the United States. The 12-month survey was conducted beginning in April 1999 by the National Center for Health Statistics (NCHS), Centers for Disease Control and Prevention (Atlanta, Georgia). This survey was designed to collect information about the health and diet.
of persons in the United States. The NHANES 99-00 is unique in that it combines a home interview with health tests that are done in a mobile examination center. The health tests consist of both physical examinations and laboratory components. The laboratory data files include findings from analyses of blood, urine, hair, air, tuberculosis skin test, and household dust specimens. Specimens were collected at the mobile examination centers or in the home. The NHANES design includes an oversampling of minority, low-income, and elderly subjects. Because of this complex sampling design, appropriate weighting factors (based on statistical stratification and population estimates) must be taken into account when calculating population-based frequency estimates. In the NHANES 99-00, 5,773 adults aged ≥18 years were interviewed and examined. By race/ethnicity, this population breaks down to 1,891 Hispanics (34.7%), 2,353 non-Hispanic Whites (43.2%), 1,049 non-Hispanic Blacks (19.3%), and 155 others (2.9%). We limited our sample of participants for this analysis to adult participants (≥17 years of age) who had serum drawn for highly sensitive CRP.

Highly sensitive CRP was measured as part of the NHANES 99-00 physical and laboratory examination. Standard phlebotomy techniques were used to obtain specimens. Serum specimens were frozen to −20°C until used for laboratory analysis. CRP was analyzed using a highly sensitive assay technique. This method quantifies CRP by latex-enhanced nephelometry. Further details about the specific method used in the laboratory procedures of the NHANES 99-00 are available on the NHANES web site (www.cdc.gov/nchs/nhanes.htm) and elsewhere.1

Elevated CRP was defined using cut-off points based on previous studies of cardiovascular disease. Our purpose was to use threshold levels that have clinical meaning as predictors of cardiovascular disease and cardiovascular events. Recently published American Heart Association guidelines have designated CRP levels >3.0 mg/L as high and as associated with increased cardiovascular risk.2 Thus, in the present study, we considered values >3.0 mg/L as elevated.

Dietary intake in the NHANES 99-00 is based on recollection of foods eaten the previous day by the respondent coupled with known nutritional content of each of these foods. The total daily dietary intake is reported for the following: fiber, total fat, saturated fatty acids, monounsaturated fatty acids, polyunsaturated fatty acids, protein, carbohydrates, total calories, and cholesterol. Fish consumption was calculated from recall of the number of times the respondent had eaten various types of fish during the previous month. These are appropriate factors for comparison to CRP values based on previous studies of diet and risk of cardiovascular disease.3,4 Each independent variable was examined by quartile in the population.

Demographic variables (age, race, gender) were included as control variables because of their known impact on CRP.5 In an effort to determine the independent relation between specific eating behaviors and CRP, additional variables were included that might influence the levels of CRP. Medications used by subjects with hypercholesterolemia and diabetes may affect CRP levels. Because such persons may also be more likely to be following a high fiber or low fat diet to treat their condition, medication use could be a confounder in the relation between diet and CRP. Thus, we controlled for taking medication for diabetes or for lowering cholesterol.6–8 We also controlled for smoking, body mass index, alcohol consumption, and exercise because of their known effects on CRP.9–11 Smoking was coded as a yes or no to current smoking (“Do you currently smoke cigarettes/cigars/pipe?”). Body mass index was calculated in the NHANES 99-00 using the weight and height data in the examination file. Alcohol consumption was calculated from responses to questions regarding frequency and amount of drinking. Exercise categories were developed from responses to questions regarding participation in moderately strenuous and vigorous activities. Because the quantity of each of the dietary factors may be linked to the total amount of food consumed, total caloric intake was incorporated as another control variable.

Because NHANES 99-00 was a complex, stratified cluster sample, standard statistical techniques could not be used. Therefore, we used SUDAAN (Research Triangle Institute, Research Triangle, North Carolina), a specialized statistical program that accounts for the complex weighting of the NHANES 99-00 sample. Using SUDAAN allowed us to correct for unequal probabilities of selection and different response rates, ensuring that the results could be generalized to the noninstitutionalized civilian population of the United States. Thus, the percentages and odds ratios (ORs) in this study represent weighted values. SUDAAN also adjusts the SEs to account for the weighting, stratifi-
consumption of associated with the risk of elevated CRP. Increased hydrate, and total caloric intake. Total calories, protein, carbohydrate use, body mass index, alcohol consumption, exercise, and total caloric intake were included in the models to control for their effects. For significant diet factors in the initial analyses, we repeated the regression analysis using the predictor as a linear variable. We also analyzed fiber and saturated fat together in 1 model to determine independent effects. Median CRP was calculated for each quartile of consumption level and compared with the lowest quartile. Standardized β, p values, ORs, and 95% confidence intervals (CI) were obtained from the logistic regression output for all models. Statistical significance was defined as ≤0.05 without correction for multiple comparisons, because there were relatively few diet factors examined and the specific analyses were planned in advance.

There were 4,900 adults included in this analysis from the NHANES population with available CRP levels. The demographics of the adult, noninstitutionalized United States population estimates derived from the NHANES respondents are listed in Table 1. The median CRP level was 2.0 mg/L (Table 2), and 64% had CRP levels ≤3.0 mg/L.

Intake/consumption data for all diet factors studied are listed in Table 2 by quartile. The relation between each diet factor and CRP is illustrated in Figure 1, adjusted for age, race, gender, smoking, medication use, body mass index, alcohol consumption, exercise, and total caloric intake. Total calories, protein, carbohydrate, fish, and cholesterol consumption were not associated with the risk of elevated CRP. Increased consumption of fiber was associated with a significantly lower likelihood of elevated CRP (Table 3). Median CRP was 23% lower in subjects in the highest quartile of fiber consumption compared with the lowest (p <0.05). When fiber was modeled as a continuous variable, increased fiber was significantly associated with a lower likelihood of elevated CRP (p <0.05). Each additional gram of fiber consumed per day was associated with a 2% lower risk of elevated CRP. For fat consumption, only the third quartile of saturated fat consumption was associated with increased likelihood of elevated CRP (OR 1.58, 95% CI 1.02 to 2.44). Consumption of other types of fat were not consistently related to greater risks of elevated CRP (Figure 1), and there was no association with saturated fat when it was modeled as a continuous variable. When fiber and saturated fat were included in the same multivariate model, only the association of lower CRP with fiber was maintained (p <0.05).

This study investigated the relation between specific diet factors and elevation of CRP. The most important finding of the present study is that increased fiber intake was significantly associated with a lower risk of having elevated CRP. This association was maintained after controlling for important factors that may have confounded the association, including age, race, gender, body mass index, smoking, alcohol consumption, exercise, medication use, and total caloric intake.

Dietary fiber and saturated fat consumption had opposite associations: greater fiber intake was associ-
ated with a beneficial decrease in risk of elevated CRP, whereas saturated fat consumption was modestly associated with an increased likelihood of elevated CRP. If confirmed in further studies, the finding that specific diet factors are associated with differences in an important cardiovascular inflammatory marker may bolster current American Heart Association diet guidelines (www.americanheart.org) that recommend high fiber fruits, vegetables, and grains, and limiting saturated fat.

Previous studies of diet and inflammatory markers have begun to reveal information about their relations, but a clear picture has not emerged. The biologic mechanisms underlying this relation are not completely elucidated but are related to the nutritional content of cofactors for enzymes that mediate the oxidative and inflammatory response in the vascular endothelium. Weight loss of ≥10% has been associated with reduction of inflammatory cytokines in a study of 56 obese women who followed a diet and exercise program for 1 year. A 2-year study in 120 obese women was also associated with lower CRP and other inflammatory markers. Whether the improvement in inflammatory markers was due to the weight loss, specific diet factors, or exercise is not clear. Stampfer and colleagues evaluated women over several years in the Nurses Health Study and found that a diet high in cereal fiber, marine omega-3 fatty acids and folate, and low in transfat and glycemic load, significantly predicted lower cardiovascular risk. However, CRP and inflammatory markers were not evaluated in that study. Fung et al evaluated the association between dietary patterns and plasma biomarkers and found that a Western diet pattern (higher in red meat, high-fat dairy products, and refined grains) was positively correlated with higher CRP. Another study that investigated dietary factors and inflammation found an inverse association between CRP and omega-3 fatty acid content of granulocyte membranes, implying that a diet higher in fish may have a protective effect on inflammatory markers. However, dietary supplementation with omega-3 fatty acids from fish oil does not reduce proinflammatory cytokines in healthy volunteers. Further, a study of 21 healthy male volunteers evaluating the impact of a Mediterranean diet on inflammatory markers showed

![FIGURE 1](image-url) Adjusted ORs of elevated highly sensitive CRP (>3.0 mg/L) risk for each quartile (Q2, Q3, and Q4) of nutrient consumption relative to the lowest quartile (Q1) for each nutrient. Error bars indicate the 95% CI.

<table>
<thead>
<tr>
<th>Dietary Fiber Quartile (g/d)</th>
<th>Unadjusted Model</th>
<th>Adjusted Model</th>
<th>Highly Sensitive CRP (mg/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR</td>
<td>95% CI</td>
<td>OR</td>
</tr>
<tr>
<td>Q1 &lt; 8.4</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>Q2 8.4–13.3</td>
<td>0.95</td>
<td>0.78–1.17</td>
<td>0.75</td>
</tr>
<tr>
<td>Q3 13.3–19.5</td>
<td>0.75</td>
<td>0.60–0.95</td>
<td>0.64</td>
</tr>
<tr>
<td>Q4 &gt; 19.5</td>
<td>0.68</td>
<td>0.55–0.84</td>
<td>0.58</td>
</tr>
</tbody>
</table>

*The median for the highest quartile is significantly lower than the median for the lowest quartile (p < 0.05). Adjusted models include age, race, gender, body mass index, smoking status, alcohol consumption, exercise, medications, and total caloric intake. Estimated United States population median highly sensitive CRP and 95% CI of the medians are shown for each quartile of fiber consumption.
no significant effect on CRP after 90 days.\textsuperscript{20} Although the explanation is unknown, the failure of the 90-day Mediterranean diet and some dietary interventions to reduce CRP in normal volunteers may reflect a “floor effect” in which it is difficult to lower normal CRP levels, or they may reflect suboptimal dietary intervention.

The findings of our study lend support to the concept that fiber may play an important role in mediating the relation between diet, inflammation, and cardiovascular disease. Further research using high fiber diets or supplements in prospective studies may provide further insight into the role of fiber in reducing inflammation associated with cardiovascular disease.


Effect of Baseline Levels on Response of High-Density Lipoprotein Cholesterol to Hypolipidemic Treatment

Genovefa D. Kolovou, MD, Deliana C. Daskalova, MD, Ilias I. Petropoulos, MD, Katherine K. Anagnostopoulou, MSc, Helen I. Bilianou, MD, Nektarios D. Pilatis, MD, Antonis N. Pavlidis, and Dennis V. Cokkinos, MD

The response of high-density lipoprotein cholesterol to hypolipidemic monotherapy with diet, statins, fibrates, or nicotinic acid was investigated prospectively in 801 patients with dyslipidemia. We hypothesized that the behavior of high-density lipoprotein cholesterol after treatment would depend on its baseline levels and the therapy used. \textcopyright 2003 by Excerpta Medica, Inc. (Am J Cardiol 2003;92:1339–1342)