Association between dietary factors and plasma adiponectin concentrations in men\textsuperscript{1–3}

Tobias Pischon, Cynthia J Girman, Nader Rifai, Gokhan S Hotamisligil, and Eric B Rimm

ABSTRACT
Background: Adiponectin, an adipocyte-derived peptide, improves insulin sensitivity, has antiinflammatory and antiatherogenic effects, and is associated with a lower risk of ischemic heart disease (IHD) and type 2 diabetes. However, little is known about dietary predictors of plasma adiponectin concentrations in humans.

Objective: Our objective was to examine cross-sectionally the association between dietary factors and plasma adiponectin in men.

Design: Our study included 532 male participants of the Health Professionals Follow-Up Study who were selected as control subjects for an investigation of biological predictors of IHD. Diet, lifestyle, and anthropometric data were assessed by questionnaires.

Results: After multivariable adjustment, adiponectin was significantly inversely related to glycemic load (−1.3 mg/L per 1-SD increase; \( P = 0.02 \)) and tended to be positively associated with total fat intake (0.7 mg/L per 0.5% of energy from fat instead of carbohydrates; \( P = 0.06 \)). We also found a significant nonlinear association between plasma adiponectin concentrations and alcohol intake (\( P \) for quadratic trend = 0.01). Thus, whereas nondrinkers had mean plasma adiponectin concentrations of 16.48 mg/L, those who consumed 0.1–4.9, 5.0–14.9, 15.0–29.9, or \( \geq 30 \) g alcohol/d had mean concentrations of 16.79 (\( P = 0.77 \) compared with nondrinkers), 18.97 (\( P = 0.02 \)), 19.11 (\( P = 0.01 \)), and 18.39 (\( P = 0.10 \)) mg/L, respectively.

Conclusions: Moderate alcohol intake is associated with higher adiponectin concentrations, whereas a carbohydrate-rich diet with a high glycemic load is associated with lower adiponectin concentrations in men with no history of cardiovascular disease. Although the strength of these associations was modest, our observations highlight the hypothesis that dietary factors may modulate plasma adiponectin concentrations—a potential mediator related to a reduced IHD risk. Am J Clin Nutr 2005;81:780–6.

KEY WORDS Obesity, nutrition, risk factors, cardiovascular disease, ischemic heart disease

INTRODUCTION
Adiponectin, a recently discovered circulating hormone secreted by the adipose tissue, is involved in glucose and lipid metabolism (1, 2). Contrary to other adipose-derived hormones, adiponectin concentrations are reduced in subjects with obesity, insulin resistance, or type 2 diabetes (1, 2). Adiponectin treatment improves insulin sensitivity in animal models, and low concentrations have been shown to predict type 2 diabetes in humans (3–7). Adiponectin is inversely associated with several traditional cardiovascular disease risk factors, such as hypertension, hypertriglyceridemia, and low HDL-cholesterol concentrations (2), and animal data suggest that adiponectin may have antiatherogenic and antiinflammatory properties (8–11). In line with these reports, high plasma concentrations were recently shown to be associated with a lower risk of ischemic heart disease (IHD) in humans, which suggests that adiponectin may be a protective mediator for this disease (12, 13).

Although studies suggest that caloric restriction, weight loss, and activation of the peroxisome proliferator activated receptor \( \gamma \) is associated with higher adiponectin concentrations (14, 15), little is known about dietary predictors of plasma adiponectin concentrations. Therefore, the aim of our study was to examine cross-sectionally the association between dietary factors and plasma adiponectin concentrations.

SUBJECTS AND METHODS
Study population
The study population comprised 532 male participants in the Health Professionals Follow-Up Study (HPFS) who were selected as control subjects in a nested case-control study of biological predictors of IHD (13). The HPFS is a prospective cohort investigation of 51,529 US male health professionals, aged 40–75 y at baseline in 1986, designed primarily to evaluate associations between diet and chronic disease incidence (16). Information about health and disease is assessed biennially, and diet is assessed every 4 y by self-administered questionnaires (17). Between 1993 and 1995, a blood sample was requested

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from all subjects; 18,225 participants provided samples. Men who provided samples were somewhat younger and smoked less, but otherwise were similar to those who did not provide samples. After exclusion of subjects with a history of cardiovascular disease before 1994, 266 subjects with incident nonfatal myocardial infarction or fatal IHD were identified during 6 y of follow-up. The control subjects were randomly selected 2:1 matched for age, date of blood drawing, and smoking status from participants with a blood sample and with no history of cardiovascular disease at the time of case ascertainment (risk-set sampling) (18). We also examined the associations between dietary factors and plasma adiponectin concentrations among cases (data not shown); however, we found no substantive differences between cases and control subjects. Because of the potential bias due to associations of adiponectin and dietary factors with IHD risk, we restricted the present analysis to the control subjects. The study protocol was approved by the Harvard School of Public Health Human Subjects Committee Review Board.

Assessment of diet, alcohol consumption, lifestyle factors, and anthropometric data

Average nutrient intakes were computed from semiquantitative food-frequency questionnaires (SFFQs) with the use of composition values primarily from US Department of Agriculture sources (19). The SFFQ used was previously evaluated for reproducibility and validity within the HPFS (17). The correlation for nutrients estimated with the SFFQs and for those measured with a 2-wk diet record ranged from 0.37 for polyunsaturated fat to 0.92 for vitamin C with supplements (average 0.65) (17). The correlations for whole foods were in a similar range. For the macronutrient intakes we used the average from the SFFQs obtained in 1986, 1990, and 1994 to minimize measurement error. The effect estimates were similar when we used information from the 1994 SFFQ only.

The average dietary glycemic index for each participant was calculated by summing the products of the carbohydrate content per serving for each food, times the average number of servings of that food per day, times its glycemic index derived from published data (20, 21), divided by the total amount of daily carbohydrate intake. The glycemic load was derived according to a similar principle, but without dividing by the total amount of carbohydrate. The performance of the SFFQ in assessing the individual foods from which the glycemic index and load were derived was previously documented (22). Furthermore, the average glycemic index and glycemic load—as assessed with these questionnaires—was previously shown to be closely related to type 2 diabetes and IHD (23, 24).

Alcohol intake was calculated by summing the frequency and amount of the alcoholic content of beer, red and white wine, and spirits as reported by the participants on the SFFQ in 1994. The alcohol content was estimated as 12.8 g/bottle or can of beer (360 mL), 11.0 g for a glass of wine (118 mL), and 14.0 g for spirits (45 mL). The reproducibility and validity of alcohol consumption measured with a self-administered questionnaire was evaluated in detail within the HPFS. Alcohol intake reported over the previous year on the SFFQ was highly correlated with the intake assessed with two 1-wk diet records (r = 0.86) (25).

Anthropometric data and smoking status were derived from the 1994 questionnaire. Physical activity was computed as the average metabolic equivalent hours, based on the types of activities and durations of activities over the previous year reported biennially on the questionnaires between 1986 and 1994. The types of activities included jogging; running; bicycling; swimming laps; playing tennis, squash, and racquetball; performing calisthenics or rowing; walking; heavy outdoor work; and weightlifting. The questionnaire included 13 response categories, ranging from 0 to 40 h/wk. One MET-h is equivalent to energy expenditure when sitting quietly for 1 h (26). Medical history was derived from the questionnaires between 1986 and 1994. Validity and reproducibility of the questionnaires and the collected data and measurements were reported in detail elsewhere (27, 28).

Measurement of biochemical variables

On arrival at our laboratory, the blood samples were centrifuged (1530 × g, 4 °C); separated into plasma, white blood cells, and red blood cells; and stored at −130 °C (or colder) in continuously alarmed and monitored liquid nitrogen freezers. Plasma adiponectin concentrations were measured by competitive radioimmunoassay (Linco Research Inc, St Charles, MO) with a CV of 3.4% (n = 39). Within the HPFS we found that adiponectin concentrations had excellent intraclass correlation coefficients over a period of 1 y and were not substantially affected by transport conditions (29). Furthermore, we found no significant correlation between plasma adiponectin concentrations and storage time (r = 0.03, P = 0.34).

Statistical analyses

Spearman’s age-adjusted partial correlation coefficients and multivariable linear regression with robust variance were used to evaluate the associations between adiponectin concentrations and dietary factors without the need of normal distribution assumptions (30). We adjusted for age (5-y categories), smoking status (never, past, nonsmoker with unknown past history, current smoker, and unknown), history of diabetes, history of hypertension, alcohol consumption (nondrinkers, 0.1–4.9 g/d, 5.0–14.9 g/d, 15.0–29.9 g/d, and ≥30 g/d), and physical activity, with and without further adjustment for body mass index (in kg/m²): <20, 20–24, 25–29, 30–34, and ≥35). In multivariate energy-density models, we additionally included total energy intake and the percentages of energy derived from protein and fat (or carbohydrate). The coefficients from these models reflect the estimated change in plasma adiponectin concentration that would result from substituting a specific percentage of energy from fat for carbohydrate (or vice versa). Dietary glycemic index and load were energy-adjusted with the use of the residual method (31) and examined in similar models that included total energy intake and energy derived from protein. The nutrients under investigation were considered as continuous variables and covaried as categorical variables (quintiles). In similar models we examined the association between alcohol consumption and plasma adiponectin concentrations by computing least-squares means. Polynomial regression and log-likelihood ratio testing were used to examine quadratic trends. The analyses were conducted with SAS (version 8.2; SAS Institute, Cary, NC), and all P values presented were two-tailed.

RESULTS

Subjects in the highest quintile of adiponectin concentrations (≥24.9 mg/L) had a lower body mass index, were physically more active, and had a higher alcohol consumption than the subjects in the lowest quintile (<10.6 mg/L) (Table 1). The
TABLE 1
Characteristics of 532 men who participated in the Health Professionals Follow-Up Study by quintiles of adiponectin concentration

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Total</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>≥24.9</th>
<th>P for trend</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adiponectin (mg/L)</td>
<td>17.9 ± 0.3 (^1)</td>
<td>7.5 ± 0.2</td>
<td>12.5 ± 0.1</td>
<td>16.5 ± 0.1</td>
<td>21.4 ± 0.2</td>
<td>31.2 ± 0.6</td>
<td>P = 0.02</td>
<td></td>
</tr>
<tr>
<td>Age (y)</td>
<td>65.2 ± 0.4</td>
<td>63.5 ± 0.8</td>
<td>66.5 ± 0.8</td>
<td>63.9 ± 0.8</td>
<td>65.1 ± 0.8</td>
<td>66.8 ± 0.8</td>
<td>P = 0.02</td>
<td></td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>25.7 ± 0.2</td>
<td>26.7 ± 0.3</td>
<td>26.6 ± 0.4</td>
<td>25.6 ± 0.4</td>
<td>24.9 ± 0.3</td>
<td>24.7 ± 0.3</td>
<td>P &lt; 0.001</td>
<td></td>
</tr>
<tr>
<td>Current smoker (%)</td>
<td>12.4</td>
<td>10.6</td>
<td>13.3</td>
<td>10.7</td>
<td>16.1</td>
<td>11.3</td>
<td>0.76</td>
<td></td>
</tr>
<tr>
<td>Physical activity (MET-hours/ wk)</td>
<td>33.9 ± 1.3</td>
<td>29.8 ± 2.2</td>
<td>28.9 ± 2.7</td>
<td>35.6 ± 3.0</td>
<td>37.6 ± 3.5</td>
<td>36.6 ± 2.7</td>
<td>P = 0.01</td>
<td></td>
</tr>
<tr>
<td>Alcohol (g/d)</td>
<td>13.5 ± 0.7</td>
<td>11.2 ± 1.6</td>
<td>11.2 ± 1.4</td>
<td>13.8 ± 1.8</td>
<td>15.4 ± 2.0</td>
<td>16.2 ± 1.6</td>
<td>0.006</td>
<td></td>
</tr>
<tr>
<td>Diabetess (%)</td>
<td>4.5</td>
<td>6.9</td>
<td>9.9</td>
<td>1.0</td>
<td>1.1</td>
<td>3.0</td>
<td>0.03</td>
<td></td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>30.8</td>
<td>41.8</td>
<td>29.2</td>
<td>26.9</td>
<td>20.6</td>
<td>31.8</td>
<td>0.12</td>
<td></td>
</tr>
<tr>
<td>Energy (kcal/d)</td>
<td>1993 ± 23</td>
<td>1989 ± 55</td>
<td>1960 ± 46</td>
<td>1976 ± 57</td>
<td>1991 ± 51</td>
<td>2040 ± 51</td>
<td>0.37</td>
<td></td>
</tr>
<tr>
<td>Protein (% of energy)</td>
<td>17.8 ± 0.1</td>
<td>18.0 ± 0.3</td>
<td>18.0 ± 0.3</td>
<td>17.9 ± 0.2</td>
<td>17.6 ± 0.2</td>
<td>17.4 ± 0.2</td>
<td>0.04</td>
<td></td>
</tr>
<tr>
<td>Carbohydrates (% of energy)</td>
<td>48.6 ± 0.3</td>
<td>48.8 ± 0.7</td>
<td>49.7 ± 0.8</td>
<td>48.8 ± 0.7</td>
<td>48.5 ± 0.8</td>
<td>47.4 ± 0.7</td>
<td>0.08</td>
<td></td>
</tr>
<tr>
<td>Total fat (% of energy)</td>
<td>31.2 ± 0.2</td>
<td>31.6 ± 0.5</td>
<td>30.5 ± 0.6</td>
<td>30.9 ± 0.5</td>
<td>30.9 ± 0.6</td>
<td>31.9 ± 0.6</td>
<td>0.50</td>
<td></td>
</tr>
<tr>
<td>Saturated fat (% of energy)</td>
<td>10.5 ± 0.1</td>
<td>10.6 ± 0.2</td>
<td>10.4 ± 0.3</td>
<td>10.2 ± 0.2</td>
<td>10.4 ± 0.3</td>
<td>10.7 ± 0.3</td>
<td>0.64</td>
<td></td>
</tr>
<tr>
<td>Monounsaturated fat (% of energy)</td>
<td>12.2 ± 0.1</td>
<td>12.4 ± 0.2</td>
<td>11.9 ± 0.2</td>
<td>12.0 ± 0.2</td>
<td>12.0 ± 0.2</td>
<td>12.5 ± 0.2</td>
<td>0.48</td>
<td></td>
</tr>
<tr>
<td>Polysaturated fat (% of energy)</td>
<td>5.7 ± 0.1</td>
<td>5.8 ± 0.1</td>
<td>5.5 ± 0.1</td>
<td>5.9 ± 0.1</td>
<td>5.7 ± 0.1</td>
<td>5.9 ± 0.1</td>
<td>0.35</td>
<td></td>
</tr>
<tr>
<td>Glycemic index (^4)</td>
<td>52.8 ± 0.1</td>
<td>53.2 ± 0.2</td>
<td>52.7 ± 0.3</td>
<td>52.9 ± 0.3</td>
<td>52.7 ± 0.2</td>
<td>52.7 ± 0.3</td>
<td>0.14</td>
<td></td>
</tr>
<tr>
<td>Glycemic load (^4)</td>
<td>128.5 ± 1.0</td>
<td>129.7 ± 2.1</td>
<td>131.4 ± 2.2</td>
<td>129.2 ± 2.0</td>
<td>127.9 ± 2.4</td>
<td>124.7 ± 2.1</td>
<td>0.04</td>
<td></td>
</tr>
</tbody>
</table>

\(^1\) All values are age-adjusted (except for age and adiponectin). MET, metabolic equivalent tasks.
\(^2\) Calculated by using the median adiponectin concentrations within quintiles as a continuous variable. The results were obtained from age-adjusted linear regression with robust variance (30).
\(^3\) \(\bar{x} \pm SD\) (all such values).
\(^4\) Energy-adjusted by using the residual method (31).

Prevalence of diabetes was slightly lower in subjects in the highest quintile of adiponectin concentrations. Protein and carbohydrate intakes and glycemic load were lower in the subjects in the highest than in the lowest adiponectin quintile. We found significant or borderline significant trends across quintiles for these variables in this age-adjusted analysis, although the mean concentrations (as shown in Table 1) suggest some deviation from linear trends.

In nonparametric correlation analyses adjusted for age (Table 2), we found a small but significant correlation for protein intake \((r = -0.10, P = 0.02)\) and alcohol consumption \((r = 0.14, P = 0.002)\) and borderline significant correlations for glycemic index \((r = -0.08, P = 0.08)\) and glycemic load \((r = -0.07, P = 0.09)\) with adiponectin concentrations.

After adjustment for age, smoking, history of diabetes and hypertension, alcohol consumption, physical activity, body mass index, energy intake, and protein intake (Table 3), a 5% increase in energy derived from carbohydrate in exchange for energy derived from fat was associated with a 0.59 mg/L decrease in plasma adiponectin concentrations \((P = 0.05)\). An increase in glycemic load of 1 SD was associated with a 1.32 mg/L decrease in adiponectin concentration \((P = 0.02)\).

In a similar multivariable-adjusted model, we found a nonlinear association between alcohol intake and plasma adiponectin concentration \((P\ for\ quadratic\ trend\ = 0.01; Figure 1)\. Thus, whereas nondrinkers \((n = 122)\) had mean plasma adiponectin concentrations of 16.48 mg/L (95% CI: 15.18, 17.78), those who consumed 0.1–4.9 \((n = 116)\), 5.0–14.9 \((n = 123)\), 15.0–29.9 \((n = 88)\), or 30 \((n = 83)\) g alcohol/d had mean concentrations of 16.79 (95% CI: 15.24, 18.33; \(P = 0.77\) compared with nondrinkers), 18.97 (95% CI: 17.23, 20.71; \(P = 0.02\)), 19.11 (95% CI: 17.47, 20.76; \(P = 0.01)\), and 18.39 (95% CI: 16.59, 20.18; \(P = 0.10\)) mg/L, respectively. These results were similar when we excluded the subjects whose alcohol intake was 50 g/d.

We also examined the relation between individual types of beverages and plasma adiponectin concentrations, with control for the other types of beverages in the multivariable-adjusted

TABLE 2
Age-adjusted Spearman partial correlation coefficients between dietary factors and adiponectin concentrations in 532 men who participated in the Health Professionals Follow-Up Study\(^3\)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>(r)</th>
<th>(P)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>0.09</td>
<td>0.05</td>
</tr>
<tr>
<td>Energy intake</td>
<td>0.03</td>
<td>0.46</td>
</tr>
<tr>
<td>Fat intake (^2)</td>
<td>0.02</td>
<td>0.65</td>
</tr>
<tr>
<td>Protein intake (^2)</td>
<td>-0.10</td>
<td>0.02</td>
</tr>
<tr>
<td>Carbohydrate intake (^2)</td>
<td>-0.06</td>
<td>0.16</td>
</tr>
<tr>
<td>Saturated fat intake (^2)</td>
<td>0.02</td>
<td>0.68</td>
</tr>
<tr>
<td>Monounsaturated fat intake (^2)</td>
<td>0.02</td>
<td>0.71</td>
</tr>
<tr>
<td>Polysaturated fat intake (^2)</td>
<td>0.04</td>
<td>0.39</td>
</tr>
<tr>
<td>Glycemic index (^4)</td>
<td>-0.08</td>
<td>0.08</td>
</tr>
<tr>
<td>Glycemic load (^4)</td>
<td>-0.07</td>
<td>0.09</td>
</tr>
<tr>
<td>Alcohol</td>
<td>0.14</td>
<td>0.002</td>
</tr>
</tbody>
</table>

\(^1\) All correlation coefficients are age-adjusted except for those between age and adiponectin.
\(^2\) Energy-adjusted.
\(^3\) Expressed as a percentage of energy intake.
\(^4\) Energy-adjusted.
TABLE 3
Multivariable-adjusted associations between macronutrient intakes and plasma adiponectin concentrations in 532 men who participated in the Health Professionals Follow-Up Study.

<table>
<thead>
<tr>
<th>Nutrient</th>
<th>Change²</th>
<th>P</th>
<th>Change²</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Energy intake (per 500 kcal/d)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total fat (per 5% of energy)</td>
<td>0.11 ± 0.37</td>
<td>0.78</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Protein (per 5% of energy)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carbohydrate (per 5% of energy)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Saturated fat (per 5% of energy)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Monounsaturated fat (per 5% of energy)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Polyunsaturated fat (per 5% of energy)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glycemic index (per 1 SD)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glycemic load (per 1 SD)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

¹ Separate models for each macronutrient. Each model includes the macronutrient, age, smoking status, history of diabetes, history of hypertension, alcohol consumption, physical activity, energy intake, and protein intake. The results were obtained from multivariable linear regression analysis with robust variance (30).

² Predicted change (±SE) in plasma adiponectin concentrations per unit increase in macronutrient intake.
³ Model includes protein and fat as macronutrients.
⁴ Model includes protein and saturated, monounsaturated, and polyunsaturated fat as macronutrients.

nondrinkers had mean plasma adiponectin concentrations of 17.76 mg/L, those who consumed 0.1–4.9, 5.0–14.9, 15.0–29.9, or ≥30 g alcohol/d had mean concentrations of 18.02 (P = 0.80 compared with nondrinkers), 18.65 (P = 0.40), 18.01 (P = 0.81), and 16.31 mg/L (P = 0.22), respectively. HDL cholesterol significantly predicted adiponectin concentrations in this model (P for linear trend < 0.001).

Additionally, we examined the established association between alcohol consumption and HDL-cholesterol concentrations to determine how strongly attenuated it might be after adjustment for adiponectin. After multivariable adjustment, there was a significant association between alcohol consumption and plasma HDL-cholesterol concentrations (P for linear trend < 0.001); mean HDL-cholesterol concentrations in the aforementioned alcohol consumption categories were as follows: 40.9 mg/dL (reference), 41.5 mg/dL (P = 0.62), 46.8 mg/dL (P < 0.001), 51.0 mg/dL (P < 0.001), and 52.4 mg/dL (P < 0.001). Further adjustment for adiponectin did not substantially change this association (P for linear trend < 0.001); the mean plasma HDL-cholesterol concentrations in the respective alcohol consumption categories were as follows: 41.6 mg/dL (reference), 42.2 mg/dL (P = 0.62), 46.4 mg/dL (P < 0.001), 50.5 mg/dL (P < 0.001), and 51.5 mg/dL (P < 0.001). In this model, adiponectin independently predicted HDL-cholesterol concentrations (P for linear trend < 0.001).

DISCUSSION

In this cross-sectional study, moderate alcohol consumption was significantly associated with higher plasma adiponectin concentrations, whereas a diet with a high glycemic load was significantly related to lower adiponectin concentrations. Carbohydrate intake also tended to be inversely related to adiponectin concentrations. Although the strength of these associations was modest, our results suggest that dietary factors are related to plasma adiponectin concentrations and support the hypothesis that dietary factors may modulate adiponectin concentrations, a potential mediator related to decreased HDL risk.
Dietary factors play an important role in the development of type 2 diabetes and IHD (32,33). Excess caloric intake contributes to the development of obesity, a major risk factor for these diseases (34). Furthermore, diets high in saturated and trans fats and with a high glycemic load (indicating a large amount of processed refined carbohydrates) increase cardiovascular disease and diabetes risk, whereas diets high in polyunsaturated fatty acids and unprocessed carbohydrates and fiber decrease such risks (35,36). Furthermore, observational and experimental data also suggest that moderate alcohol intake reduces the risk of type 2 diabetes and IHD (37–39). Changes in blood lipid composition, which are well-established risk factors for IHD, only partially explain the effects of diet and alcohol on IHD risk (40). Our observations highlight adiponectin as one novel mediator for the effects of diet on chronic diseases.

Thus far, few studies on the dietary predictors of plasma adiponectin concentrations have been conducted. In animal models, caloric restriction and weight loss were associated with an increase in plasma adiponectin concentrations (41), and it was recently reported that conjugated linoleic acid increases adipose tissue messenger RNA expression and plasma concentrations of adiponectin in obese animal models after 8 wk of feeding (42). In contrast, Polson and Thompson (43) found no effect of diet macronutrient composition on adiponectin messenger RNA expression in white adipose tissue of rats. Xu et al (44) found that chronic intake of high amounts of alcohol, which lead to alcoholic liver disease, may decrease adiponectin concentrations in mice. In our analysis, adiponectin tended to be slightly lower in subjects who consumed >15.0 g alcohol/d than in those who consumed 5.0–14.9 g/d; however, because our study included only a limited number of subjects with a very high alcohol consumption, it is not clear whether a high alcohol intake is associated with a further decrease in adiponectin concentrations.

In humans, Esposito et al (14) found in a randomized controlled trial that a Mediterranean-style diet and increased physical activity, aimed at reducing body weight, significantly decreased body mass index and concomitantly increased plasma adiponectin concentrations in postmenopausal obese women. Yannakoulia et al (45) found no significant association between macronutrient intake and plasma adiponectin concentrations in a cross-sectional analysis of 114 students after multivariable adjustment. However, food intake in their study was measured by using 3-d food records, which may be less accurate in reflecting long-term dietary intake. Arvidsson et al (46) found no significant differences in adiponectin concentrations between obese women who consumed for 10 wk a hypocaloric moderate-fat, moderate-carbohydrate diet and those who consumed a low-fat, high-carbohydrate diet. However, despite reductions in body weight, this study also failed to show significant accompanying changes in adiponectin concentrations, which may have been due to the limited power of the study or to the fact that the intervention in this study was too short.

Adiponectin shows only a small degree of circadian variability (47) and, therefore, is supposedly involved in long-term rather than short-term regulatory mechanisms (48). In line with these observations, there is only limited within-person variation in plasma adiponectin concentrations over time (29). Also consistent with these findings are data from Peake et al (49), who reported no changes in plasma adiponectin concentrations during the 6 h after intake of a high-fat low-carbohydrate meal. Recently, Sierksma et al (50) examined the effect of alcohol consumption (40 g whiskey/d) on plasma adiponectin concentrations in a randomized crossover trial. They found significantly greater plasma adiponectin concentrations after the consumption, for 17 d, of whiskey (8.78 mg/L) than of water (7.94 mg/L). Taken together, these data and the results of the present study suggest that adiponectin concentrations are unlikely to be affected by acute dietary changes, but rather reflect dietary intakes over more chronic time periods.

Our study had some limitations. The cross-sectional design limited causal inferences; however, the SFQ was obtained before the blood samples were drawn; thus, reverse causality seems unlikely. The mechanisms that link moderate alcohol consumption to increased adiponectin concentrations are unclear. Although this association was somewhat attenuated after adjustment for HDL-cholesterol concentrations in our cross-sectional analysis, data from Sierksma et al (50) suggest that adiponectin concentrations change independently of HDL-cholesterol concentrations in response to alcohol intake, which indicates that adiponectin is not just a marker of HDL-cholesterol concentrations. Furthermore, we cannot exclude the possibility that adiponectin is merely a marker of insulin sensitivity; however, as indicated above, experimental data suggest that it is rather upstream of insulin resistance in the metabolic pathway. We used body mass index instead of waist-hip ratio to assess abdominal obesity; therefore, we cannot exclude the possibility of residual confounding. Dietary intake was based on self-report; however, measurement error from using self-reported dietary intake and lifestyle variables has been shown to be relatively small (17,28) and likely does not bias our results because reporting error is not likely associated with the biological measurements. Although the present study does not represent a random sample of the US population, the ranges of anthropometric variables and the biological measures are quite broad and comparable with those of the general male population. Nevertheless, future studies should address dietary predictors of adiponectin concentrations in women. It is currently unknown whether the long-term storage of blood samples affects plasma adiponectin concentrations; however, adiponectin concentrations were not significantly related to storage time in our population, and storage time is unlikely to be related to dietary factors. Adiponectin concentrations may be elevated in patients with overt diabetic nephropathy (51); however, our analysis included a minority of men with diabetes (4.5%), we adjusted for the history of diabetes, and we found essentially the same results when we excluded men with diabetes from our analysis.

In conclusion, we found that moderate alcohol intake is associated with significantly higher adiponectin concentrations, whereas a diet with a high glycemic load was significantly associated with carbohydrate intake tended to be associated with lower adiponectin concentrations. Although the strength of these associations was modest, our observations highlight the hypothesis that dietary factors may modulate plasma concentrations of adiponectin, a potential mediator related to reduced IHD risk.
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