Plasma Saturated and Linoleic Fatty Acids Are Independently Associated With Blood Pressure
Sameline Grimsgaard, Kaare H. Bønaa, Bjarne K. Jacobsen and Kristian S. Bjerve

Hypertension. 1999;34:478-483
doi: 10.1161/01.HYP.34.3.478

Hypertension is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1999 American Heart Association, Inc. All rights reserved.
Print ISSN: 0194-911X. Online ISSN: 1524-4563

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://hyper.ahajournals.org/content/34/3/478

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Hypertension can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Hypertension is online at:
http://hyper.ahajournals.org//subscriptions/
Plasma Saturated and Linoleic Fatty Acids Are Independently Associated With Blood Pressure

Sameline Grimsgaard, Kaare H. Bønaa, Bjarne K. Jacobsen, Kristian S. Bjerve

Abstract—The role of individual fatty acids in blood pressure regulation is unclear. We studied the cross-sectional relationship of blood pressure, total plasma phospholipid fatty acid concentrations, and proportions of individual fatty acids among participants in a population study. Blood pressure was measured automatically, and plasma phospholipid fatty acids were determined by gas-liquid chromatography in 4033 healthy men 40 to 42 years old. Significant positive linear associations existed between total fatty acids and saturated fatty acids and blood pressure, whereas polyunsaturated linoleic acid was inversely associated with blood pressure. In multiple regression analyses, a 2-SD increase in total fatty acids was associated with an increase of 6.0 (95% CI, 5.1 to 6.8) mm Hg systolic blood pressure. A 2-SD increase in saturated palmitic acid was associated with a 1.4 (95% CI, 0.5 to 2.3) mm Hg increase in systolic blood pressure. In contrast, a 2-SD increase in polyunsaturated linoleic acid was associated with a 1.9 (95% CI, 1.0 to 2.8) mm Hg decrease in systolic blood pressure. We conclude that plasma levels of total fatty acids, saturated fatty acids, and polyunsaturated linoleic acid are independently associated with blood pressure. The present study supports the hypothesis that the composition of dietary fat influences blood pressure. (Hypertension. 1999;34:478-483.)

Key Words: fatty acids ■ blood pressure ■ human

The relationship between dietary fats and blood pressure is controversial. Systolic blood pressure was positively correlated with dietary saturated fat in ecological data.1 Observational studies that indicate that dietary saturated fat is positively associated with blood pressure2-4 and polyunsaturated fat and the polyunsaturated/saturated fat (P/S) ratio are inversely associated with blood pressure2,3,5 contradict reports that found no such associations.6,7

Blood levels of fatty acids may be used to examine the relationship between individual fatty acids and blood pressure. There are reports of positive associations between blood pressure and blood levels of saturated and monounsaturated fatty acids,8-10 whereas polyunsaturated fatty acids have been both positively and inversely associated with blood pressure.8,10 Most previous studies included selected study groups9,10 or few subjects.8,10 On the basis of experimental data in animals and humans, 1 review found that n-6 polyunsaturated fatty acids decrease blood pressure in hypertensive individuals.11 However, 2 reviews of observational data and clinical trials concluded that dietary fats do not influence blood pressure levels.12,13

Plasma levels of essential polyunsaturated fatty acids reflect dietary intake,14,15 whereas plasma levels of nonessential fatty acids are less reliable indicators of dietary fat. Nevertheless, plasma levels of palmitic acid (16:0) and stearic acid (18:0) and monounsaturated fatty acids correlated with dietary saturated fat.14,15 In addition, high levels of dihomo-gamma-linolenic acid (20:3n-6) may reflect a diet rich in saturated fat.16

We analyzed the association between plasma levels of phospholipid fatty acids and blood pressure in 4033 men 40 to 42 years old. The large sample size provided enough information to evaluate the independent associations of total fatty acids and individual fatty acids with blood pressure.

Methods

Subjects and Measurements

All men and women 40 to 42 years old who lived in Nordland County, Norway, were invited in 1988-1989 to a health screening organized by the National Health Screening Service, the University of Tromsø (Norway), and the local health authorities.17 Plasma phospholipid fatty acids were quantified in a substudy of men, of whom 5492 were invited and 4302 (78%) participated. In our analysis, we excluded men who reported previous myocardial infarction (n=19), use of antihypertensive drugs (n=104), or both (n=7) and men whose blood pressure (n=1) or plasma fatty acid (n=138) measurements were unavailable.

The health screening invitation included a questionnaire on cardiovascular disease, smoking habits, and leisure time physical activity (3 levels).18 A second questionnaire, which included questions on alcohol consumption,19 was distributed at the screening and returned via mail by 3483 men. Data on alcohol consumption were available for 3396 men. The study was approved by the Norwegian Data Inspectorate, which considered the legal and ethical issues of the study, and the subjects gave informed consent.
Body weight was measured on an electronic scale with subjects dressed in lightweight clothing. Height was measured in centimeters. Body mass index (BMI) was calculated as the body weight in kilograms divided by the square of the height in meters (kg/m\(^2\)). We measured blood pressure by the oscillometric method\(^{20}\) with an automatic device (Dinamap, Critikon).\(^{17}\) After the subject had rested for 2 minutes, 3 recordings were made at 1-minute intervals with the individual sitting. The lowest blood pressure value was used in the analysis.

A nonfasting blood sample was analyzed for serum cholesterol at the Central Laboratory, Ulleval Hospital, Oslo.\(^{21}\) Plasma phospholipid fatty acids (myristic acid [14:0], 16:0, 18:0, arachidic acid [20:0], behenic acid [22:0], lignoceric acid [24:0], palmitoleic acid [16:1], oleic acid [18:1], gondoic acid [20:1], erucic acid [22:1], nervonic acid [24:1], eicosatrienoic acid [20:3n-9], linoleic acid [18:2n-6], eicosadienoic acid [20:2n-6], 20:3n-6, arachidonic acid [20:4n-6], adrenic acid [22:4n-6], linolenic acid [18:3n-3], eicosapentaenoic acid [20:5n-3], docosapentaenoic acid [22:5n-3, 22:5n-6], and docosahexaenoic acid [22:6n-3]) were quantified by gas-liquid chromatography as described previously.\(^{22}\) The coefficients of variation for individual fatty acids estimated from replicate analyses (\(n=55\)) ranged from 3.3% to 6.6%. Fatty acids were measured as \(\mu\)mol/L and relative concentrations, mol%. Trans-fatty acids were not measured.

### Statistical Analysis

All variables were normally distributed except 20:5n-3, which was log-transformed. Pearson and Spearman correlation coefficients were computed to evaluate unadjusted relationships between fatty acids and blood pressure, BMI, total cholesterol, daily smoking, physical activity, and alcohol consumption. Total fatty acids and individual fatty acids that showed significant univariate associations with blood pressure were included in multiple regression analyses. We included fatty acids associated with dietary saturated fat (16:0, 16:1, and 20:3n-6), dietary n-6 (18:2n-6), and dietary n-3 polyunsaturated fat (20:5n-3) and also examined possible contributions of other fatty acids. Finally, we adjusted for BMI, daily smoking, physical activity, and alcohol consumption. Residual analyses confirmed the model assumptions. Logistic regression was used to estimate the odds ratio for hypertension (defined as systolic blood pressure \(\geq 160\) mm Hg and/or diastolic blood pressure \(\geq 95\) mm Hg) by a 2-SD change in fatty acid concentrations. Two-sided \(P<0.05\) was considered statistically significant. The SAS software package was used (SAS Corp).\(^{23}\)

### Results

Ten percent of the study participants (Table 1) were hypertensive. Saturated, monounsaturated, n-6, and n-3 fatty acids accounted for 44%, 11%, 35%, and 10% of total fatty acids, respectively. The most abundant saturated, monounsaturated, and n-6 fatty acids were 16:0, 18:1, and 18:2n-6, respectively (Table 2). Monounsaturated and polyunsaturated fatty acids displayed larger interindividual variability than did levels of saturated fatty acids. The correlations between individual and total fatty acids were generally weak (data not shown). Levels of 16:0, 16:1, 18:1, 20:3n-9, and 20:3n-6 acids were positively intercorrelated (\(r=0.10\) to 0.53) and were inversely correlated with 18:2n-6 (\(r=-0.08\) to \(-0.36\)). Very-long-chain n-3 fatty acids were inversely correlated with levels of n-6 fatty acids (\(r=-0.18\) to \(-0.65\)). Total fatty acids were highly correlated with serum total cholesterol (\(r=0.72\)).

Blood pressure was positively associated with total fatty acids (Table 2). Mean systolic blood pressure increased by 10 mm Hg from the bottom to the top decile of total fatty acid concentration, without any evidence of a threshold level below which or a plateau above which there was no association (Figure 1, top left). Levels of 18:2n-6 were inversely associated with blood pressure: mean systolic blood pressure decreased by 6 mm Hg from the bottom to the top decile of the 18:2n-6 concentration (Figure 1, bottom left). Systolic blood pressure was also positively associated with levels of 16:0, 16:1, 18:1, 20:3n-9, 20:3n-6, and 20:5n-3 (Table 2 and Figure 1, right).

Total fatty acids and relative concentrations of 16:0 and 18:2n-6 were independently associated with blood pressure in multiple regression analysis (Table 3, model 1). Models 2 to 4 show the relationship between systolic blood pressure and fatty acids when we substituted 16:0 with 16:1 and 20:3n-6, which also are considered to reflect dietary saturated fat. All 3 fatty acids showed highly significant independent positive relationships with systolic blood pressure. When fatty acids were added one at a time, no fatty acids other than 16:0, 16:1, and 20:3n-6 were significantly associated with systolic blood pressure when total fatty acids and 18:2n-6 were already included in the regression models. In addition, total fatty acids, 16:0, and 18:2n-6 remained significantly associated with blood pressure when we controlled for BMI, physical activity, smoking, and alcohol consumption (Table 3, model 5). Fatty acids were similarly associated with systolic and diastolic blood pressure (data not shown). The regression model, which included total fatty acids, 16:0, and 18:2n-6, explained 6% and 9% of the variability in systolic and diastolic blood pressure, respectively. The association between levels of 18:2n-6 and diastolic blood pressure was stronger than that of systolic blood pressure and remained significant after adjustment for BMI.

Figure 2 (top) illustrates the independent association of total fatty acids and BMI with blood pressure. The prevalence of hypertension was 23% among the 605 men in the top tertile of total fatty acids and BMI. In contrast, 3% of the 576 men in the bottom tertile of total fatty acids and BMI were...
hypertensive. Total fatty acids and 18:2n-6 were independently associated with blood pressure (Figure 2, bottom). The prevalence of hypertension was 21% among 532 men in the top tertile of total fatty acids and bottom tertile of 18:2n-6. In contrast, 4% were hypertensive among the 528 men in the bottom tertile of total fatty acids and top tertile of 18:2n-6. By multiple logistic regression in which we controlled for BMI, daily smoking, alcohol consumption, and physical activity,

### TABLE 2. Levels of Plasma Phospholipid Fatty Acids and Correlations With Systolic Blood Pressure, BMI, Smoking, Physical Activity, and Alcohol Consumption in 4033 Men

<table>
<thead>
<tr>
<th>Fatty Acid</th>
<th>Mean ± SD</th>
<th>CV* (%)</th>
<th>Systolic Blood Pressure†</th>
<th>BMI†</th>
<th>Daily Smoking‡</th>
<th>Physical Activity‡§</th>
<th>Alcohol Consumption‡§</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total fatty acids, μmol/L</td>
<td>4523 ± 682</td>
<td>15</td>
<td>0.23</td>
<td>0.23</td>
<td>-0.09</td>
<td>-0.09</td>
<td>0.18</td>
</tr>
<tr>
<td>Mol%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>16:0</td>
<td>26.6 ± 1.54</td>
<td>6</td>
<td>0.09</td>
<td>0.11</td>
<td>-0.02</td>
<td>-0.03</td>
<td>0.28</td>
</tr>
<tr>
<td>18:0</td>
<td>13.9 ± 0.93</td>
<td>7</td>
<td>-0.03</td>
<td>0.11</td>
<td>0.02</td>
<td>0.00</td>
<td>-0.21</td>
</tr>
<tr>
<td>16:1</td>
<td>0.37 ± 0.18</td>
<td>49</td>
<td>0.17</td>
<td>0.17</td>
<td>-0.01</td>
<td>-0.06</td>
<td>0.23</td>
</tr>
<tr>
<td>18:1</td>
<td>8.52 ± 1.24</td>
<td>15</td>
<td>0.06</td>
<td>-0.05</td>
<td>-0.12</td>
<td>-0.04</td>
<td>0.10</td>
</tr>
<tr>
<td>20:3n-9</td>
<td>0.11 ± 0.07</td>
<td>64</td>
<td>0.10</td>
<td>0.11</td>
<td>-0.03</td>
<td>-0.05</td>
<td>0.13</td>
</tr>
<tr>
<td>18:2n-6</td>
<td>23.5 ± 3.62</td>
<td>15</td>
<td>-0.12</td>
<td>-0.25</td>
<td>-0.10</td>
<td>0.04</td>
<td>-0.17</td>
</tr>
<tr>
<td>20:3n-6</td>
<td>2.45 ± 0.67</td>
<td>27</td>
<td>0.09</td>
<td>0.30</td>
<td>0.04</td>
<td>-0.09</td>
<td>0.00</td>
</tr>
<tr>
<td>20:4n-6</td>
<td>7.87 ± 1.40</td>
<td>18</td>
<td>0.02</td>
<td>0.13</td>
<td>0.06</td>
<td>-0.04</td>
<td>0.10</td>
</tr>
<tr>
<td>18:3n-3</td>
<td>0.18 ± 0.09</td>
<td>50</td>
<td>0.02</td>
<td>-0.06</td>
<td>-0.04</td>
<td>0.03</td>
<td>-0.01</td>
</tr>
<tr>
<td>20:5n-3</td>
<td>2.37 ± 1.73</td>
<td>73</td>
<td>0.07</td>
<td>0.11</td>
<td>0.08</td>
<td>0.04</td>
<td>0.10</td>
</tr>
<tr>
<td>22:6n-3</td>
<td>6.52 ± 1.66</td>
<td>26</td>
<td>0.03</td>
<td>0.09</td>
<td>0.17</td>
<td>0.04</td>
<td>0.04</td>
</tr>
</tbody>
</table>

*Coefficients of variation.
†Pearson and ‡Spearman coefficients: absolute values >0.03, 0.04, and 0.05 are significant at P<0.05, P<0.01, and P<0.001, respectively.
§See Table 1 for categories of physical activity and alcohol consumption.
Includes 14:0, 16:0, 18:0, 20:0, 22:0, 24:0, 16:1, 18:1, 20:1, 22:1, 24:1, 20:3n-9, 18:2n-6, 20:2n-6, 20:3n-6, 20:4n-6, 22:4n-6, 22:5n-6, 18:3n-3, 20:5n-3, 22:5n-3, and 22:6n-3.

Figure 1. Top left, Mean systolic blood pressure by deciles of total fatty acids in plasma phospholipids (μmol/L). Bottom left, Mean systolic blood pressure by deciles of 18:2n-6 in plasma phospholipids (mol%). Right, Mean systolic blood pressure by deciles of 16:0, 16:1, and 20:3n-6 acids in plasma phospholipids (mol%). Error bars denote 95% CI.
the odds ratio for hypertension was 2.2 (95% CI, 1.7 to 2.7) for a 2-SD increase in total fatty acids and 0.6 (95% CI, 0.5 to 0.8) for a 2-SD increase in 18:2n-6.

**Discussion**

We found a strong positive and linear relationship between the total amount of plasma phospholipid fatty acids and blood pressure. To the best of our knowledge, this association has not been examined in previous reports. Concentrations of fatty acids associated with dietary saturated fat (16:0, 16:1, and 20:3n-6) were positively associated with blood pressure, and there was an inverse relationship between the concentration of polyunsaturated 18:2n-6 and blood pressure. These associations were independent in multivariate analyses. Our findings are strengthened by the population-based study design, the relatively high participation rate, and the large sample size. However, because we studied men 40 to 42 years old who consumed a Western diet, the results need confirmation in other age groups and in women.

The association between plasma phospholipid fatty acids and blood pressure was independent of BMI. A positive relationship between dietary saturated fat and blood pressure independent of BMI has been found in some but not all population studies. Earlier clinical trials were small and had methodological problems. However, a recent controlled trial [the Dietary Approaches to Stop Hypertension (DASH) study] reported a modest reduction in blood pressure independent of BMI in subjects who were fed a diet formulated to reduce saturated fat (although intake of cholesterol, calcium, and protein were slightly altered versus the other experimental diet). BMI is a strong determinant of blood pressure. Part of the association between BMI and blood pressure may depend on dietary fat. Therefore, it can be questioned whether adjustment for BMI is appropriate when assessing the strength of the relationship between dietary fat, as reflected in plasma fatty acids, and blood pressure.

We found that plasma concentrations of 16:0, 16:1, and 20:3n-6 were positively associated with blood pressure. Other investigators have found dietary and plasma levels of 18:2n-6 to be inversely associated with blood pressure, but the results are inconsistent. The possibility of detecting a relationship between 18:2n-6 and blood pressure may be limited by low interindividual variation, imprecise measures of dietary 18:2n-6, small sample size, and the degree of statistical control for potential confounders.

**Table 3. Multiple Linear Regression Analysis of Systolic Blood Pressure in 4033 Men**

<table>
<thead>
<tr>
<th>Predictor Variable</th>
<th>Model 1</th>
<th>Model 2</th>
<th>Model 3</th>
<th>Model 4</th>
<th>Model 5*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total fatty acids, μmol/L†</td>
<td>6.0 (5.1, 6.8)</td>
<td>5.3 (4.4, 6.2)</td>
<td>5.8 (5.0, 6.7)</td>
<td>5.8 (4.9, 6.6)</td>
<td>4.9 (3.9, 5.9)</td>
</tr>
<tr>
<td>16:0, mol%</td>
<td>1.4 (0.5, 2.3)</td>
<td>1.1 (0.1, 2.1)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>16:1, mol%</td>
<td></td>
<td>2.5 (1.6, 3.4)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>18:2n-6, mol%</td>
<td>−1.9 (−2.8, −1.0)</td>
<td>−1.6 (−2.5, −0.7)</td>
<td>−2.3 (−3.1, −1.4)</td>
<td>−1.7 (−2.6, −0.8)</td>
<td>−1.0 (−2.0, −0.1)</td>
</tr>
<tr>
<td>20:3n-6, mol%</td>
<td>1.5 (0.6, 2.3)</td>
<td>2.0 (1.1, 2.9)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sum of 16:0, 16:1, and 20:3n-6, mol%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>4.8 (3.9, 5.8)</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.6 (0.0, 1.3)</td>
</tr>
<tr>
<td>Physical activity 1 to 3‡</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.0 (−0.5, 0.6)</td>
</tr>
<tr>
<td>Alcohol consumption‡</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.1 (−1.0, 1.0)</td>
</tr>
<tr>
<td>Daily smoking, no/yes</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Adjusted $R^2$ 0.06 0.06 0.06 0.06 0.08

Values are estimated mean change (95% CI) in systolic blood pressure (mm Hg) by 2-SD or 1-category increase in predictor variable.

* $n=3394$.
† See Table 2 for individual fatty acids included in total fatty acids.
‡ See Table 1 for categories of physical activity and alcohol consumption.
We found that plasma levels of n-3 fatty acids were positively associated with blood pressure in crude analysis, but no consistent relationship existed in the multivariate analyses. Blood pressure was positively associated with plasma 20:5n-3 concentrations in a small study of Finnish men. In contrast, blood pressure was inversely associated with plasma 20:5n-3 in mildly hypertensive individuals. A meta-analysis concluded that marine n-3 fatty acids in pharmacological doses have a hypotensive effect, which is restricted to hypertensive subjects and individuals with atherosclerosis.

Plasma levels of 18:2n-6 and n-3 polyunsaturated fatty acids reflect dietary intake. However, levels of saturated and monounsaturated fatty acids may reflect both dietary fat and endogenous fat synthesis. The concentrations of saturated fatty acids displayed little variation among the men in our study and indicated that levels of saturated fat in plasma phospholipids are actively regulated. Nevertheless, in populations that consume diets high in saturated fat, blood levels of saturated and monounsaturated fatty acids were associated with dietary saturated fat, probably because of their common sources in milk products and animal fat. Blood levels of 20:3n-6 increased on a diet high in saturated fat and low in 18:2n-6. These data suggest that high levels of 16:0, 16:1, and 20:3n-6 reflect a diet high in saturated fat relative to polyunsaturated fat.

A limitation when interpreting relative concentrations of fatty acids is that if the dietary intake of 1 fatty acid increases, the relative concentrations of some other fatty acids may decrease. However, in the present analysis, the associations of saturated and polyunsaturated fatty acids with blood pressure remained significant in multivariate analyses, which suggests that we observed true independent associations. Given the lack of dietary data and the crude measures of physical activity and alcohol use in the present study, we cannot exclude the possibility of residual confounding by lifestyle variables. However, the question of physical activity segregated groups according to physical fitness, and the measure of alcohol use was strongly associated with levels of γ-glutamyltransferase and usual alcohol consumption in a population study conducted in the same geographical area as the present study.

The extent to which total plasma phospholipid fatty acids reflect fat metabolism or dietary fat is unknown. There was a strong positive association between the concentration of total fatty acids and total cholesterol, and dietary saturated fat is the main lifestyle determinant of total cholesterol levels. We hypothesize that total fatty acids partly reflect dietary total fat and saturated fat intake.

The mechanisms by which fatty acids may influence blood pressure remain unknown. In humans, blood pressure and cardiac β-adrenergic receptor responsiveness decreased on a low-fat diet with a high P/S ratio. A high fat meal reduced brachial artery reactivity, which suggested that fatty acids influence blood pressure by modulating endothelial function. Dietary saturated fat may also promote atherosclerosis and arterial stiffening and thereby increase blood pressure. Carotid intima thickness was positively associated with blood levels of saturated fat. Animal studies suggest that 18:2n-6 may reduce blood pressure by serving as a substrate for vasoactive prostaglandins and promote relaxation of vascular smooth muscle cells.

This study showed that plasma phospholipid total fatty acids and the proportions of saturated fatty acids and 18:2n-6 were independently associated with blood pressure and suggested that fatty acids are involved in blood pressure regulation. Additional studies are needed to determine whether these associations reflect cause-and-effect relations and whether blood pressure can decrease on a diet low in total and saturated fat and high in polyunsaturated 18:2n-6.

Acknowledgments

This study was financially supported by the Norwegian Research Council and was conducted in collaboration with the National Health Screening Service, Oslo, Norway.

References


