Plasma Fatty Acid Composition as a Predictor of Arterial Stiffness and Mortality

Simon G. Anderson, Thomas A.B. Sanders, J. Kennedy Cruickshank

Abstract—Aortic stiffness predicts cardiovascular mortality and may be influenced by dietary fat composition. The hypothesis that plasma fat composition influences arterial stiffness and subsequent mortality was tested here in a prospective study. A total of 174 randomly sampled nondiabetic participants aged 45 to 74 years were recruited from local populations, stratified by ethnicity and gender, and followed up for mortality. Aortic pulse wave velocity (PWV), blood pressure, and fatty acid composition of plasma lipids were measured at baseline. PWV was associated with increased cardiovascular mortality and inversely related to the proportions of docosahexaenoic (ρ=−0.22; P=0.02) and arachidonic acids (ρ=−0.25; P<0.001) in plasma lipids. Principal component analyses identified a cluster characterized by higher proportions of palmitate, palmitoleic and oleic acid and lower proportions of linoleic, dhexo-γ linoleic, and arachidonic acids. This cluster was positively associated with PWV, central adiposity, smoking, and increased mortality (hazard ratio: 1.13; 95% CI: 1.01 to 1.27). A second cluster, with higher proportions of arachidonic, eicosapentaenoic, and docosahexaenoic and lower proportions of oleic, palmitic, and linoleic acid levels, was associated with lower PWV and systolic blood pressure but also decreased risk of mortality (hazard ratio: 0.57; 95% CI: 0.39 to 0.82), independent of PWV and blood pressure. These data suggest that plasma fatty acid profiles characterized by a higher proportion of long-chain polyunsaturated fatty acids are associated with decreased cardiovascular mortality, independent of the impact of aortic PWV. The results are consistent with an effect of dietary sources of n-3 long-chain polyunsaturates influencing arterial stiffness and mortality. (Hypertension. 2009;53:839-845.)

Key Words: blood flow ■ blood flow velocity ■ vasculature ■ fatty acids ■ mortality

A diet high in saturated fatty acids and low in polyunsaturated fatty acids is associated with increased risk of atherosclerosis in humans and, experimentally, causes atherosclerosis in nonhuman primates.1 With increasing age, arteries stiffen because of loss of elasticity, increased arterial calcification, and progressive atherosclerosis.2 Arterial stiffness has emerged as a strong predictor of cardiovascular mortality.3–5 The effect of dietary fatty acid intake on arterial stiffness has been only studied to a limited extent. Hamazaki et al6 were among the first to report differences in arterial compliance among inhabitants of a Japanese fishing village, which had a low rate of cardiovascular disease, compared with a farming village that had a high rate. This difference was attributed to the long-chain n-3 polyunsaturated fatty acids found in fish, in particular eicosapentaenoic acid (20:5n-3; EPA) and docosahexaenoic acid (22:6n-3; DHA). The initial observation was confirmed in a follow-up study.7 Wahlqvist et al8 found an association between arterial stiffness and fish consumption in a cross-sectional study of diabetic patients in Australia. The assessment of large artery stiffness by determining, generally, aortic pulse wave velocity (PWV) has been well validated and has been widely used in the cohort studies.

Despite evidence of an inverse relationship between intakes of linoleic acid and long-chain n-3 polyunsaturated fatty acids with mortality,9,10 studies linking plasma fatty acid composition and mortality are sparse.11 The fatty acid composition of total plasma lipids is a reliable marker of the intake of linoleic acid and long-chain n-3 polyunsaturated fatty acids.12–14 We have also established that, in these northwest London communities, there were clear differences in dietary intakes between ethnic groups, notably, very little long-chain polyunsaturated acids because of no fish intake in vegetarians.15 In our previous report, differences in arterial stiffness predicted mortality across the range of glucose tolerance in this community.16 The relationship between patterns of plasma polyunsaturated fatty acid composition and arterial stiffness has not been investigated. We tested the hypothesis that baseline fatty acid composition of total plasma lipids would not only be related to arterial stiffness at baseline but also to subsequent mortality in an ethnically diverse prospective cohort with different patterns of fat intake.
Methods

A random sample of people aged 45 to 74 years was drawn from population registers held in 2 northwest London health centers, stratified by age and gender in 1987 to 1988. The study included the 3 main local ethnic groups: people of European, African-Caribbean, or Gujarati Indian origin. Ethnic group defined by self-reported grandparental origin (≥3 of 4 grandparents in a particular group), anthropometric, and other details were described earlier.17 A subset of 174 participants without known diabetes mellitus, selected randomly, had PWV measurements. Follow-up was via tagging of death certificates at the Office of National Statistics (now National Health Service Information Centre) in the United Kingdom. Their quarterly reports recorded dates and causes of death or emigration, here censored at March 31, 2008. Research ethics approval for the study and mortality follow-up were obtained from appropriate research ethics committees at Northwick Park and Central Middlesex hospitals.

Laboratory Assays

Blood was collected, centrifuged within 2 hours of test completion, separated, and plasma frozen at −70°C until analysis. Plasma cholesterol, high-density lipoprotein cholesterol, triglyceride, and nonesterified fatty acid concentrations, measured in whole plasma by an automated enzymic assay, and fatty acid composition of total plasma lipids were determined on blood collected into lithium heparin at baseline and measured within 6 months of collection, as described previously.14 Fatty acid methyl esters were separated on a 25-m CPSiI88 capillary column (Chromopak) by using hydrogen as the carrier gas in a split ratio of 50:1. Chromatograms were integrated on a Shimadzu CR1 B integrator (Dyson Instruments). Fatty acid methyl esters were identified by comparison with authentic standards obtained from Sigma and expressed as absolute amounts of total fatty acid esters (weight percentage). An internal standard of pentadecanoic acid was used to facilitate the quantification of fatty acid concentrations.

Arterial Stiffness

Arterial stiffness, measured at baseline, was determined by measuring aortic PWV using Doppler probes, as described previously.16 Briefly, 2 continuous-wave Doppler probes were used, one clamped at the base of the left side of the neck to insonate the root of the left subclavian artery and the other used to insonate the abdominal aorta, above its bifurcation in participants lying flat for >5 minutes. This maximized vessel length for the waveforms while minimizing reflection artifacts from smaller resistance-vessel beds. Signals from the foot of the proximal to the foot of the distal waveform generated transit times over the measured cutaneous distance (sternoclavicular notch to distal probe), giving PWV (meters per second). The

<table>
<thead>
<tr>
<th>Variable</th>
<th>Alive at Follow-Up</th>
<th>Died</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ethnicity, n</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White Europeans</td>
<td>26 28</td>
<td></td>
<td>F=25.6; P=0.0001</td>
</tr>
<tr>
<td>African Caribbean</td>
<td>39 7</td>
<td></td>
<td>NS</td>
</tr>
<tr>
<td>Gujarati Indians</td>
<td>49 25</td>
<td></td>
<td>NS</td>
</tr>
<tr>
<td>Gender, male/female, n</td>
<td>57/59 32/26</td>
<td></td>
<td>NS</td>
</tr>
<tr>
<td>Age, y</td>
<td>58.7 (57.7 to 59.8) 63.6 (62.1 to 65.1)</td>
<td>F=25.6; P=0.0001</td>
<td></td>
</tr>
<tr>
<td>Height, cm</td>
<td>1.62 (1.61 to 1.64) 1.64 (1.61 to 1.66)</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>26.6 (25.9 to 27.4) 25.7 (24.7 to 26.7)</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>Waist:hip ratio</td>
<td>0.89 (0.88 to 0.90) 0.89 (0.87 to 0.91)</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>SBP, mm Hg</td>
<td>136 (132 to 140) 146 (141 to 152)</td>
<td>F=8.25; P=0.0046</td>
<td></td>
</tr>
<tr>
<td>Diastolic BP, mm Hg</td>
<td>78 (76 to 80) 82 (79 to 85)</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>PWV, m/s</td>
<td>9.8 (9.4 to 10.2) 10.8 (10.2 to 11.4)</td>
<td>F=6.33; P=0.01</td>
<td></td>
</tr>
<tr>
<td>Total HDL, mmol/L</td>
<td>1.29 (1.22 to 1.35) 1.16 (1.06 to 1.24)</td>
<td>F=5.05; P=0.03</td>
<td></td>
</tr>
<tr>
<td>Total cholesterol, mmol/L</td>
<td>5.5 (5.4 to 5.7) 5.6 (5.3 to 5.8)</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>Triglycerides, mmol/L</td>
<td>1.36 (1.20 to 1.52) 1.74 (1.50 to 1.98)</td>
<td>F=6.19; P=0.02</td>
<td></td>
</tr>
<tr>
<td>Oleic acid, 18:1*</td>
<td>18.5 (17.8 to 19.3) 20.2 (18.9 to 21.1)</td>
<td>F=4.62; P=0.033</td>
<td></td>
</tr>
<tr>
<td>DHA, 22:6n-3*</td>
<td>1.9 (1.7 to 2.2) 1.4 (1.1 to 1.8)</td>
<td>F=4.53; P=0.035</td>
<td></td>
</tr>
</tbody>
</table>

Smoked status, %

- Never: 74.7 25.3 χ²=12.28; P=0.002
- Ex-smoker: 33.3 66.6
- Current smoker: 58.3 41.7

On oral antihypertensives, n

- No: 97 42 NS
- Yes: 19 16

Glucose intolerant, n (%)†

- No: 82 (69) 37 (31) NS
- Yes: 34 (62) 21 (38)

Data are means (95% CIs) or proportions (%). Comparisons were made, as appropriate, using the χ² for categorical variables and AVOA for continuous variables. HDL indicates high-density lipoprotein; NS, not significant.

*Data were adjusted for ethnicity, age, and gender.
†Glucose intolerant was defined as having impaired glucose tolerance/impaired fasting glucose or type 2 diabetes mellitus.
Spearman coefficients and mortality analyses with person-years of analyzed. Model numbers varied depending on the variables in analyses. Components derived from each sample, but the rest were not and were then used to determine the number of factors to retain. The first 5 factor scores were calculated for each individual, extracted, and used as much of the remaining variance of all of the fatty acids as possible. For the 10 measured plasma fatty acids, it allows a description of the major fatty acid patterns in the data. Using the “pca” command in Stata, the factor loadings for the components and factor scores were calculated for each individual, extracted, and used for analyses. A higher score indicated that individuals had a fatty acid pattern described by the component more commonly than those with a lower score. The “mineigen” and the “fapara” commands were used to determine the number of factors to retain. The first 5 components were highly correlated with their corresponding component derived from each sample, but the rest were not and were then excluded from the remaining analysis. Each individual’s age, ethnicity, and gender were included with the 10 fatty acids in these analyses.

Not all of the measurements were obtained on all of the individuals, accounting for the discrepancies in the numbers of individuals analyzed. Model numbers varied depending on the variables included, with any missing values leading the participant to be dropped from the model.

### Results

A total of 174 participants had PWV measured at baseline. Those who died were older, with higher mean systolic BP (SBP; 146 versus 136 mm Hg), and had 10% greater PWV (mean difference: 1.8 m/s; 95% CI: 1.0 to 2.6 m/s; Table 1). We found no significant differences in age- and gender-adjusted PWV by ethnic group (African Caribbeans: 10.1 m/s [95% CI: 9.4 to 10.7 m/s]; Europeans: 9.7 m/s [95% CI: 9.1 to 10.3]; and Gujaratis: 10.5 m/s [95% CI: 9.9 to 11.0 m/s]), in PWV by smoking status (10.1 m/s [95% CI: 9.6 to 10.6 m/s] in nonsmokers versus 10.2 m/s [95% CI: 9.6 to 10.9 m/s] in current or ex-smokers, or by BMI category.

### Plasma Fatty Acid Composition

Palmitic acid (16:0) and linoleic acid (18:2n-6) were the most abundant fatty acids in plasma lipids. Compared with Europeans (Table 2), African Caribbeans had higher proportions of arachidonic acid (20:4n-6; AA), EPA (20:5n-3), and DHA (all P<0.0001). Linoleic acid was highest in Gujaratis who were vegetarian (P<0.0001). Values were higher for palmitoleic (16:1) and oleic acid (18:1n-9) in Europeans. Adjusting for age, gender, and ethnicity, participants in the highest when compared with the lowest tertile of DHA had the lowest PWV (11.1 m/s [95% CI: 10.3 to 11.8 m/s] versus 9.7 m/s [95% CI: 8.9 to 10.5 m/s]; F=3.68; P=0.02), Figure 1 shows the distribution of fatty acid levels by ethnicity and tertile of PWV (minimum: 8.59 m/s; middle: 8.60 to 10.56 m/s; maximum: 10.57 m/s). The proportion of DHA was lowest in Gujaratis, especially in the highest tertile of PWV. EPA was highest in African-Caribbean subjects. After adjusting for age, gender, and ethnic group, the proportion of DHA (22:6n-3) was lower in those who died, but that of oleic acid was higher. No differences were noted in comparisons using the other fatty acids.

### Correlations With Fatty Acid Composition

DHA (r=−0.22; P=0.02) and AA (r=−0.25; P=0.007) were inversely related to PWV, but no relationship was found with EPA, dihomo-γ-linoleic (20:3n-6), linoleic, oleic, or stearic acids. In partial correlation analyses, the correlations between PWV and DHA (r=−0.18; P=0.047), as well as AA (r=−0.17; P=0.07), were borderline independent of age, gender, and ethnic group. There were no significant correlations between SBP and individual fatty acids.

### PWV and Other Metabolic Indices

As expected, there were highly significant positive relationships between PWV and age (r=0.56; P<0.0001), SBP (r=0.57; P<0.0001), and diastolic BP (r=0.25; P=0.0007). The relationships were weak with fasting glucose (r=0.13;
P = 0.09), nonesterified fatty acid (r = 0.14; P = 0.09), and triglycerides (r = 0.14; P = 0.07) and inverse with height (r = −0.14; P = 0.07) and apolipoprotein A1 (r = −0.20; P = 0.07). There were no relationships between PWV and waist or with levels of total high-density lipoprotein, low-density lipoprotein cholesterol, triglyceride, fibrinogen, or factor VIIc.

Principal Component Analyses
Principal component analyses, including ethnicity, age, gender, and the 10 major fatty acids, identified 5 components that explained 71.6% of the variation in these variables in the study population (please see the data supplement available online at http://hyper.ahajournals.org). For example, component 4, characterized by higher proportions of AA, EPA, and DHA and lower proportions of linoleic, oleic, and palmitic acids (Figure 2), was inversely related to PWV (r = −0.46; P < 0.0001), SBP (r = −0.33; P < 0.0001), and smoking (r = −0.25; P = 0.001; Table 3).

Mortality
Participants were followed-up for a median of 19.6 years (2983 person-years) with 58 recorded deaths (in 174 participants [33%]), 34 from cardiovascular causes. Crude mortality rates for both genders combined were 20.0 (95% CI: 15.5 to 25.9) deaths per 1000 person-years overall, 31.9 (95% CI: 21.7 to 46.8) in European (26 deaths), and 19.9 (95% CI: 13.4 to 29.4) and 8.5 (95% CI: 4.0 to 17.8) per 1000 person-years in Gujarati and African-Caribbean subjects (25 and 7 recorded deaths), respectively. Those in the highest tertiles of PWV (> 10.6 m/s) had greater mortality (Figure 3A). Participants in the upper tertiles of oleic and palmitic acids had greater mortality rates (adjusted to the mean age of 60 years) than those in the lowest tertiles. Conversely, those in the upper tertiles of EPA (20:5n-3) and DHA (22:6n-3) had better age-adjusted survival estimates (Figure 3B).

Relationship Between Mortality and Fatty Acid Component
The pattern of higher polyunsaturated fatty acid and lower saturated fatty acids (component 4) was associated with reduced mortality (hazard ratio [HR]: 0.49 [95% CI: 0.39 to 0.82]) in a univariate Cox regression analysis. In addition, risk of all-cause mortality was halved with component 4 (HR: 0.57 [95% CI: 0.39 to 0.82]), separate of the independent impact of PWV (HR: 1.15 [95% CI: 1.01 to 1.30] per m/s), SBP (1.02 [95% CI: 1.01 to 1.04] per mm Hg), or smoking status (HR: 1.98 [95% CI: 0.99 to 3.97] ever smoked) in Cox regression analyses. Component 1, characterized by higher proportions of 16:0, 16:1, and 18:1 but lower proportions of 18:2n-6, 20:3n-6, and 20:4n-6 (Figure 2), was associated with increased mortality (HR: 1.13 [95% CI: 1.01 to 1.27]) in univariate analyses. However in multivariate analyses with PWV, SBP, or smoking status, there were no statistically significant relationships.

The analyses were repeated in those with cardiovascular deaths (34 of 174 participants), and the Cox regression models also indicated a 50% reduction in mortality from cardiovascular deaths with component 4 (HR: 0.44 [95% CI: 0.27 to 0.67]; P = 0.001). This association was independent of PWV, SBP, and smoking. There was no relationship with component 1.

Discussion
Most previous studies relating arterial stiffness to increased mortality have been conducted in older subjects with hypertension or overt vascular disease (renal and coronary). The
EPA and DHA do not lower serum cholesterol and are cholesterol compared with unsaturated fatty acids. However, has been demonstrated that the latter 2 fatty acids raise serum acids myristic and palmitate were related to increased risk. It that intake of the saturated fatty was convincing evidence for a protective effect of linoleic years. The World Health Organization concluded that there between reported fatty acid intakes and arterial stiffness has been published by a few studies, the impact of actual fatty acid composition on PWV has not. One study by Nishizawa et al showed an independent inverse relationship correlation between the EPA concentrations in the red blood cell phospholipid fraction and PWV between the brachia and ankles. The results that we report are consistent with the previous evidence and provide a mechanism through which these fatty acids may act.

The role of fat composition in relation to risk of cardiovascular disease has been a subject of intense debate for >50 years. The World Health Organization concluded that there was convincing evidence for a protective effect of linoleic acid, EPA, and DHA and that intake of the saturated fatty acids myristic and palmitate were related to increased risk. It has been demonstrated that the latter 2 fatty acids raise serum cholesterol compared with unsaturated fatty acids. However, EPA and DHA do not lower serum cholesterol and are believed to affect the risk of cardiovascular disease by effects on vascular function. Dietary linoleic acid is known to lower low-density lipoprotein cholesterol with high proportions of linoleic acid in serum cholesteryl esters inversely related to cardiovascular disease and total mortality. A meta-analysis assessing the effects of n-3 fatty acid intake on cardiovascular and total mortalities found substantial variations between studies, with the pooled estimate showing no clear evidence of reduced risk.

High intakes of saturated fatty acids combined with a low linoleic acid result in increases in the proportions of palmitic, palmitoleic, and oleic acids. In contrast, the proportions of EPA and DHA in plasma lipids are determined mainly by intake of preformed DHA, especially from fish, but are negatively influenced by the intake of linoleic acid. The conversion of α-linolenic acid to DHA is not a major determinant of variations in the proportion of DHA in plasma lipids. AA is synthesized from linoleic acid more efficiently but may also be obtained from meat and fish. There were marked differences between the ethnic groups in fatty acid composition. The high proportions of linoleic acid in the Gujarati subjects who were all vegetarians reflect high intakes of linoleic acid-rich vegetable oils. Higher proportions of EPA and DHA among African Caribbeans are likely to be derived from fish. The markedly lower DHA in Gujaratis is consistent with a vegetarian diet virtually devoid of this fatty acid.

PCA here identified different clusters of dietary fat composition and then associated these clusters with arterial stiffness and all-cause mortality. Although the relationship between reported fatty acid intakes and arterial stiffness has been published by a few studies, the impact of actual fatty acid composition on PWV has not. One study by Nishizawa et al showed an independent inverse relationship correlation between the EPA concentrations in the red blood cell phospholipid fraction and PWV between the brachia and ankles. The results that we report are consistent with the previous evidence and provide a mechanism through which these fatty acids may act.

We identified a cluster of fatty acids where the proportions of 16:0, 16:1, and 18:1 were greater, whereas those of 18:2 n-6, 20:3 n-6, and 20:4 n-3 were lower. This pattern would be

![Factor loadings (eigenvalues) for given fatty acids](image)

**Figure 2.** Comparison of 2 clusters from PCA. The clusters (components) have patterns characterized by higher or lower proportions of saturated and polyunsaturated fatty acids. Component 4 with higher proportions of AA (20:4 n-6), EPA (20:5 n-3), and DHA (20:3 n-6) and lower saturated fatty acids is associated with lower PWV and decreased mortality. The factor loadings are eigenvalues. Higher eigenvalues suggest more of the particular fatty acid than those with lower or negative values.

### Table 3. Spearman Rank Correlation Coefficients of the 5 Fatty Acid Principal Components With Anthropometric and Metabolic Variables

<table>
<thead>
<tr>
<th>Variable</th>
<th>Component 1</th>
<th>Component 2</th>
<th>Component 3</th>
<th>Component 4</th>
<th>Component 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>PWV, m/s</td>
<td>0.07</td>
<td>0.20*</td>
<td>−0.03</td>
<td>−0.46*</td>
<td>0.19</td>
</tr>
<tr>
<td>Ever smoked</td>
<td>0.31†</td>
<td>−0.05</td>
<td>−0.06</td>
<td>−0.25†</td>
<td>−0.33†</td>
</tr>
<tr>
<td>Waist circumference</td>
<td>0.08</td>
<td>0.19*</td>
<td>−0.24*</td>
<td>−0.04</td>
<td>−0.23*</td>
</tr>
<tr>
<td>Waist:hip ratio</td>
<td>0.24*</td>
<td>−0.03</td>
<td>−0.18*</td>
<td>−0.07</td>
<td>0.08</td>
</tr>
<tr>
<td>SBP, mm Hg</td>
<td>0.05</td>
<td>−0.06</td>
<td>−0.14</td>
<td>−0.36†</td>
<td>0.02</td>
</tr>
<tr>
<td>Diastolic BP, mm Hg</td>
<td>0.11</td>
<td>−0.17*</td>
<td>−0.13</td>
<td>−0.16*</td>
<td>−0.11</td>
</tr>
<tr>
<td>Fasting glucose, mmol/L</td>
<td>0.01</td>
<td>0.05</td>
<td>−0.15*</td>
<td>−0.01</td>
<td>−0.03</td>
</tr>
<tr>
<td>2-h glucose, mmol/L</td>
<td>−0.12</td>
<td>0.27*</td>
<td>−0.12</td>
<td>−0.04</td>
<td>0.01</td>
</tr>
</tbody>
</table>

Data are Spearman correlations coefficients (r) and were unadjusted for other variables. If the presented correlation coefficient (r) has no footnote, then the P value is not statistically significant.

P values for the significance level of the correlation coefficients are *P<0.05 or †P<0.001.
that expected on a diet with a low polyunsaturated:saturated fatty acid ratio and would be associated with increased risk of death from coronary heart disease, as in many earlier reports. A second cluster was identified, characterized by high proportions of EPA, AA, and DHA, that was associated with decreased PWV and SBP but a markedly low risk of all-cause mortality independent of PWV.

High intakes of long-chain n-3 fatty acids lower BP, but the intakes used in such intervention studies (in excess of 3 g/d) are way beyond the amounts consumed in diets. An open-label, 1-year intervention of 1.8 g of EPA per day by Tomiyama et al reported a 0.33-m/s reduction in PWV. Arterial stiffness increases slowly with increasing age, with the annual rate of increase at the age of 60 years being in the order of 0.4 m/s per year (T.A.B.S., P.J. Chowienczyk, unpublished observations, 2004); it is possible that diets containing moderate amounts of oily fish may retard arterial stiffening over longer periods.

The findings presented here are novel and important but are limited by the small sample size and its consequent impact via possible type 2 errors. The analytic method used, PCA, is a widely applied tool used to summarize common patterns of variation among groups of variables. One of its disadvantages is that the estimated total variance calculated is not separated into common or unique variance; rather, the component is a complex function of the variables.

In conclusion, plasma fatty acid composition, particularly a pattern of higher polyunsaturated fatty acid and lower saturated fatty acids, appears to predict cardiovascular mortality independent of the impact of PWV. The results here support current recommendations to reduce the intake of saturated fatty acids. The data also suggest that long-chain polyunsaturated fatty acids or their dietary source (oily fish) have an independent effect on decreasing mortality.

**Perspectives**

Mechanisms controlling vascular tone are influenced by dietary factors, with qualitative differences in types of dietary fat emerging as potentially important. Fish oil fatty acids modulate vascular reactivity postprandially, potentially improving vascular tone. The data suggest that, across groups with different dietary fat patterns, individuals with higher plasma long-chain polyunsaturated fatty acids, eg, EPA (20:5n-3) and DHA (22:6n-3), not only have lower arterial stiffness as measured by PWV but also have slower mortality over long-term follow-up compared with those with traditional profiles higher in saturated fatty acids. The effects are likely to be either direct on endothelial metabolism or by altering membrane structural properties across the vascular wall.

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**Disclosures**

None.

**References**


13. Sanders TA, Lewis F, Slaughter S, Griffin BA, Griffin M, Davies I, Millward DJ, Cooper JA, Miller GJ. Effect of varying the ratio of n-6 to n-3 fatty acids by increasing the dietary intake of alpha-linolenic acid, eicosapentaenoic and docosahexaenoic acid, or both on fibrinogen and clotting factors VII and XII in persons aged 45–70 y: the OPTILIP Study. *Am J Clin Nutr.* 2006; 84: 513–522.


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PLASMA FATTY ACID COMPOSITION AS A PREDICTOR OF ARTERIAL
STIFFNESS AND MORTALITY

Running title: Fatty acid composition and arterial stiffness

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Online supplement word count (excluding title page): 151
## Table S1. Factor loadings of the fatty acids in the five principal components of fatty acid combinations identified

<table>
<thead>
<tr>
<th>Variable</th>
<th>Component 1</th>
<th>Component 2</th>
<th>Component 3</th>
<th>Component 4</th>
<th>Component 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Variation explained (%)</td>
<td>25.6</td>
<td>15.8</td>
<td>11.5</td>
<td>10.1</td>
<td>8.7</td>
</tr>
<tr>
<td><strong>Myristic</strong> (14:0)</td>
<td>0.17</td>
<td>0.34</td>
<td>-0.23</td>
<td>0.46</td>
<td>0.05</td>
</tr>
<tr>
<td><strong>Palmitic</strong> (16:0)</td>
<td>0.36</td>
<td>0.35</td>
<td>0.06</td>
<td>0.05</td>
<td>-0.07</td>
</tr>
<tr>
<td><strong>Palmitoleic</strong> (16:1)</td>
<td>0.47</td>
<td>0.10</td>
<td>0.00</td>
<td>-0.05</td>
<td>0.20</td>
</tr>
<tr>
<td><strong>Stearic</strong> (18:0)</td>
<td>0.01</td>
<td>0.12</td>
<td>0.50</td>
<td>0.32</td>
<td>0.16</td>
</tr>
<tr>
<td><strong>Oleic</strong> (18:1)</td>
<td>0.45</td>
<td>-0.05</td>
<td>0.03</td>
<td>-0.13</td>
<td>-0.06</td>
</tr>
<tr>
<td><strong>Linoleic</strong> (18:2n-6)</td>
<td>-0.45</td>
<td>0.23</td>
<td>0.11</td>
<td>-0.19</td>
<td>-0.17</td>
</tr>
<tr>
<td><strong>Dihomo-gamma-linoleic</strong> (20:3n-6)</td>
<td>-0.13</td>
<td>-0.14</td>
<td>-0.45</td>
<td>0.04</td>
<td>0.62</td>
</tr>
<tr>
<td><strong>Arachidonic</strong> (20:4n-6)</td>
<td>-0.27</td>
<td>-0.25</td>
<td>0.29</td>
<td>0.30</td>
<td>0.08</td>
</tr>
<tr>
<td><strong>Eicosapentaenoic</strong> (20:5n-3)</td>
<td>0.06</td>
<td>-0.43</td>
<td>-0.34</td>
<td>0.22</td>
<td>0.08</td>
</tr>
<tr>
<td><strong>Docosahexaenoic</strong> (22:6n-3)</td>
<td>0.08</td>
<td>-0.54</td>
<td>0.20</td>
<td>0.04</td>
<td>-0.20</td>
</tr>
<tr>
<td><strong>Ethnicity (compared with Europeans)</strong></td>
<td>-0.34</td>
<td>0.35</td>
<td>-0.18</td>
<td>0.14</td>
<td>0.07</td>
</tr>
<tr>
<td><strong>Age</strong></td>
<td>-0.01</td>
<td>0.03</td>
<td>0.10</td>
<td>-0.67</td>
<td>0.36</td>
</tr>
<tr>
<td><strong>Gender (= compared with Men)</strong></td>
<td>0.02</td>
<td>0.01</td>
<td>0.46</td>
<td>0.12</td>
<td>0.57</td>
</tr>
</tbody>
</table>

*Higher factor loadings (eigenvalues) suggest more of the particular fatty acid than those with lower or negative eigenvalues.*