Factor analysis of fatty acids in serum lipids as a measure of dietary fat quality in relation to the metabolic syndrome in men\textsuperscript{1–3}

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ABSTRACT
Background: A specific fatty acid (FA) composition in plasma lipid esters is related to the metabolic syndrome (MetS) and may influence the development of the MetS.

Objective: The objective was to define and study FA factors as measures of dietary fat quality and endogenous FA metabolism in relation to MetS.

Design: Principal factor analysis was performed to define specific FA factors in men participating in a population-based cohort study—the Uppsala Longitudinal Study of Adult Men. The factors were generated at ages 50 (n = 2009) and 70 (n = 576) y, and relations between FA factors and MetS (National Cholesterol Education Program) were studied in cross-sectional and prospective (20 y) analyses.

Results: The factor analysis generated 3 major FA factors: a low-linoleic acid (LA) factor, a dietary saturated FA factor, and an n−3 polyunsaturated FA (PUFA) factor. All factors differed between those subjects with MetS (n = 281 of 2009) and those without MetS at age 50 y; only the low-LA factor differed at age 70 y, which suggests an association between MetS and fat quality. The low-LA factor (odds ratio: 1.51; 95% CI: 1.28, 1.79; P < 0.0001) and the n−3 PUFA factor (0.76; 0.64, 0.90; P < 0.001) predicted MetS development over 20 y, independent of smoking habits, physical activity, and BMI.

Conclusions: The generated FA factors, which presumably represent dietary fat quality and endogenous FA metabolism, may be important in the development of MetS. This finding supports current dietary recommendations to increase PUFA intake and restrict saturated FA intake.

KEY WORDS Factor analysis, fat quality, Δ-desaturase, metabolic syndrome, National Cholesterol Education Program, NCEP

INTRODUCTION

The metabolic syndrome (MetS) is characterized by the clustering of risk factors and is associated with an increased risk of cardiovascular disease and type 2 diabetes. It typically includes abdominal obesity, hypertension, insulin resistance resulting in impaired glucose metabolism, and dyslipidemia. Several etiologic factors are involved in the development of MetS, including genetic predisposition and lifestyle factors (1). Diet and physical inactivity are environmental factors that might promote several of the components of MetS. A high intake of fat may influence the progression of obesity, and dietary fat quality may affect insulin sensitivity (2–4).

The fatty acid (FA) composition of serum lipid esters [cholesteryl esters (CEs) and phospholipids] mirrors dietary FA intakes over the previous few weeks and also reflects endogenous FA metabolism (5–8), for which different enzymes, such as desaturases and elongases, play an important role (3). Consequently, the FA composition in serum lipids can be used as a biomarker of fat quality, but also as an indicator of disease risk (9), because an altered FA composition has been related to metabolic disease and cardiovascular disorders in observational and intervention studies (2, 4). High concentrations of palmitic acid (16:0) and low concentrations of linoleic acid (LA) (18:2n−6) in plasma lipid esters and proportionally higher concentrations of palmitoleic (16:1n−7) and dihomo-γ-linolenic (20:3n−6) acids are characteristic of persons with such an altered FA pattern. Also, the activities of Δ-desaturases [Δ\textsuperscript{9−} or stearoyl CoA desaturase (SCD), Δ\textsuperscript{6}-desaturase (D6D), and Δ\textsuperscript{5}-desaturase (D5D)], which can be estimated by using the product-to-precursor FA ratios, are usually altered (3).

Intervention studies have shown that the FA pattern in plasma changes after substituting saturated FAs (SFAs) for monounsaturated FAs (MUFAs) or carbohydrates (4, 10), which results in improved insulin sensitivity (11). It has also been observed that a diet rich in SFAs induces the same FA pattern in serum lipid esters as seen in persons with MetS (4, 10).

The amount of FAs in serum CEs is expressed as a percentage of total FAs and is a relative measure. This means that many of the FAs are intercorrelated and that a change in the proportion of one FA will influence the proportions of several others. We therefore used a principal component analysis to define certain serum FA factors that could be regarded as indicators of fat quality, endogenous FA metabolism, or both and then to relate the factors to the development of MetS. We believe it is easier to grasp the concept of fat-quality factors than to consider the entire
FA composition of serum lipid esters when discussing FA in relation to disease risk. The aims of the present study were to define specific serum FA factors and then to investigate the cross-sectional relations between the generated FA factors and MetS and its components and to study the predictive role of FA factors in the development of MetS over 20 y.

SUBJECTS AND METHODS

Subjects

The participants in the present study were taking part in a population-based cohort study, the Uppsala Longitudinal Study of Adult Men (ULSAM). This study started in Uppsala, Sweden, in 1970 and all men born between 1920 and 1924 and living in Uppsala were invited to take part. The participants were examined at baseline at age 50 y and were reinvestigated at the ages of 60, 70, 77, and 82 y (ongoing; Internet: http://www.pubcare.uu.se/ULSAM/). In the present study we analyzed data from the 576 at ages 50 and 70 y, respectively. The total number of study subjects with complete FA data were 2009 and 18:3n-6/18:2n-6, and D5D = 20:4n-6/20:3n-6. From this point forward in the text, the ratios of 16:1n-7 to 16:0 and of 18:1n-9 to 18:0 will be referred to as Δ9-16 and Δ9-18, respectively.

Investigations at age 50 y

All investigations were performed under standardized conditions and were described in detail previously (12, 13). The investigations included a medical questionnaire, an interview, blood sampling, anthropometric measurements, and blood pressure (BP) measurements. Supine BPs were recorded with a mercury manometer while the subjects were in a recumbent position. Blood samples were drawn after an overnight fast, and triacylglycerol, HDL-cholesterol, serum CE FA, and serum fasting insulin and blood glucose concentrations were measured. Body mass index (BMI) was calculated as weight (in kg) divided by height squared (in m). CE FA composition was analyzed as previously described (14, 15). Serum was extracted with a hexane-isopropanol solution, and CEAs were separated from the extract by thin-layer chromatography before interesterification with acidic methanol. Free cholesterol that had been liberated in the reaction was removed by aluminum oxide to avoid contamination of the column. The composition of methylated FAs was determined by gas chromatography (a 25-m NB-351 silica capillary column) with a flame ionization detector and helium as carrier gas. Smoking habit was considered a categorical variable, where nonsmoker = 0, smoker = 1, and exsmoker = 2. Physical activity levels were graded 1–4, where 1 was the lowest and 4 the highest activity level.

Investigations at age 70 y

The measurements at age 70 y were performed in a manner similar to those at age 50 y and are described in detail elsewhere (16, 17). Triacylglycerol, HDL-cholesterol, serum CE FA, and serum fasting insulin and blood glucose concentrations were measured; anthropometric and BP measurements were also made. A medical questionnaire was used, and an interview was conducted. The FA composition was analyzed according to procedures previously described (14). However, the gas-liquid chromatograph (GLC) system used was different at age 70 y than at age 50 y. The GLC system consisted of a Hewlett-Packard (Avondale, PA) GC 5890 with an automatic sampler (model 7671A) and an integrator (model 3392A) and a 25-m Quadrex (New Haven, CT) fused silica capillary column (model OV-351). The FAs were identified by comparing each peak’s retention time with the retention times of NuChek Prep’s (Elysian, MN) methyl ester standards (GLC reference standard GLC-68A).

Estimation of desaturase activity

The desaturase activity was estimated as the ratio of product to precursor of individual FAs in serum CE according to the following: SC-D-1 = 16:1n-7/16:0 and 18:1n-9/18:0, D6D = 18:3n-6/18:2n-6, and D5D = 20:4n-6/20:3n-6. From this point forward in the text, the ratios of 16:1n-7 to 16:0 and of 18:1n-9 to 18:0 will be referred to as Δ9-16 and Δ9-18, respectively.

Definition of the metabolic syndrome

We used the National Cholesterol Education Program’s (Adult Treatment Panel III) definition of MetS (1), because it is the most recently suggested and practical definition to use in the clinical setting. MetS was considered present when ≥3 of the following risk factors were met: fasting plasma glucose ≥6.1 mmol/L, systolic BP ≥130 mm Hg or diastolic BP ≥85 mm Hg or antihypertensive medication use, triacylglycerol ≥1.69 mmol/L, HDL cholesterol <1.04 mmol/L, or waist circumference >102 cm. Waist circumference was only recorded for those persons born in 1920 and 1921 (n = 480); thus, the obesity criteria at age 50 y was defined as a BMI >29.4, which corresponded to a waist circumference >102 cm [linear regression equation: BMI = 0.298 × waist circumference (cm) - 1.027]. Of the 70-y-old men, waist circumference was measured for most men (n = 1192), and the original definition was used.

Statistical analysis

The statistical analysis was performed with the use of the software package STATA (version 8.2; STATA Corporation, College Station, TX). The normal distribution of the continuous variables was examined with Shapiro-Wilk’s test, and skewed variables were log transformed. To determine how FAs in serum CE as well as estimated SCD, D6D, and D5D activities relate to one another, we performed a principal component analysis in which the FAs 16:0, 16:1, 18:0, 18:1, 18:2n-6, 18:3n-6, 18:4n-6, 20:3n-6, 20:4n-6, 20:5n-3, and 22:6n-3 and the estimated desaturase activities were entered in the analysis. The resulting factor pattern was interpreted by using factor loadings, and the most powerful factors (eigen values >1.0) were retained for further analysis. Factor loadings >0.5–0.6 were considered to be of importance. Descriptive results are presented as means ± SDs. Differences in means were explored by analysis of variance. Tests for trend between the numbers of MetS criteria in relation to the factor 1 score were carried out by using linear regression analysis. Cross-sectional and prospective univariate and multivariate logistic regression analysis was performed with the different factor scorings as independent variables at age 50 y and were adjusted for BMI, smoking habit, and physical activity.
TABLE 1
Average proportions of fatty acids in serum cholesteryl esters and estimated desaturase activities at ages 50 and 70 y in subjects with and without the metabolic syndrome (MetS)1.

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Age 50 y</th>
<th>Age 70 y</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>MetS (n = 281)</td>
<td>No MetS (n = 1728)</td>
</tr>
<tr>
<td>% of total fatty acids</td>
<td>% of total fatty acids</td>
<td></td>
</tr>
<tr>
<td>16:0 (palmitic acid)</td>
<td>12.2 ± 1.02</td>
<td>11.6 ± 0.96</td>
</tr>
<tr>
<td>16:1 (palmitoleic acid)</td>
<td>4.3 ± 1.32</td>
<td>3.8 ± 1.3</td>
</tr>
<tr>
<td>18:0 (stearic acid)</td>
<td>1.26 ± 0.32</td>
<td>1.15 ± 0.3</td>
</tr>
<tr>
<td>18:1 (oleic acid)</td>
<td>20.0 ± 2.52</td>
<td>19.4 ± 2.8</td>
</tr>
<tr>
<td>18:2n−6 (linoleic acid)</td>
<td>51.9 ± 4.92</td>
<td>54.3 ± 5.2</td>
</tr>
<tr>
<td>18:3n−6 (γ-linolenic acid)</td>
<td>0.80 ± 0.312</td>
<td>0.70 ± 0.30</td>
</tr>
<tr>
<td>18:3n−3 (α-linolenic acid)</td>
<td>0.66 ± 0.16</td>
<td>0.66 ± 0.16</td>
</tr>
<tr>
<td>20:3n−6 (dihomo-γ-linolenic acid)</td>
<td>0.64 ± 0.142</td>
<td>0.56 ± 0.13</td>
</tr>
<tr>
<td>20:4n−6 (arachidonic acid)</td>
<td>4.9 ± 1.0</td>
<td>4.8 ± 0.9</td>
</tr>
<tr>
<td>20:5n−3 (eicosapentaenoic acid)</td>
<td>1.36 ± 0.66</td>
<td>1.35 ± 0.62</td>
</tr>
<tr>
<td>22:6n−3 (docosahexaenoic acid)</td>
<td>0.69 ± 0.20</td>
<td>0.70 ± 0.21</td>
</tr>
<tr>
<td>Ratio of 16:1−7 to 16:0 (Δ9−16)</td>
<td>0.36 ± 0.102</td>
<td>0.33 ± 0.11</td>
</tr>
<tr>
<td>Ratio of 18:1−9 to 18:0 (Δ9−18)</td>
<td>16.7 ± 4.22</td>
<td>17.7 ± 4.6</td>
</tr>
<tr>
<td>Ratio of 18:3n−6 to 18:2n−6 (Δ6D)</td>
<td>(16 ± 7)2</td>
<td>(13 ± 6)</td>
</tr>
<tr>
<td>Ratio of 20:4n−6 to 20:3n−6 (Δ5D)</td>
<td>7.8 ± 2.02</td>
<td>8.7 ± 2.0</td>
</tr>
</tbody>
</table>

1 All values are ± SD.
2 P < 0.0001 (ANOVA).
3 P < 0.001 (ANOVA).
4 P < 0.05 (ANOVA).
5 Values are × 10−3.

(singly and in combination). P values <0.05 were considered significant.

RESULTS

Prevalence of MetS

The prevalence of MetS in the total ULSAM population was 14% (315/2322) and 24% (289/1221) at ages 50 and 70 y, respectively. The prevalence among those with complete FA data were not significantly different, 14% (281/2009) at age 50 y and 26% (147/576) at age 70 y, which suggests that the subsamples with complete FA data were representative.

Proportions of fatty acids, estimated desaturase activities, and MetS

The proportions of FAs in serum CE and estimated desaturase activities differed significantly between those subjects who had MetS and those who did not (Table 1). The proportions of 16:0, 16:1, 18:1, 18:3n−6, 20:3n−6, Δ9−16, and Δ6D were significantly higher, at the same time as 18:2n−6 and DSD were significantly lower in subjects with MetS at the ages of 50 and 70 y; 18:0 was higher and Δ9−18 lower in subjects with MetS at 50 y of age only, whereas 20:4n−6 was higher at age 70 only.

Factor loadings of the proportions of fatty acids and estimated desaturase activities

At age 50 y, the most powerful factor (eigen value = 4.97) comprised mainly positive loadings from the proportions of 16:1, 18:1−9, 18:3n−6, Δ9−16, and Δ6D activities as well as an inverse loading of 18:2n−6 (Table 2). This factor was called the "low LA" factor. Factor 2, denoted the "dietary SFA" factor, comprised mainly positive loadings from the proportions of 16:0, 18:0, and inverse loadings from Δ9−18 and Δ9−16 (to a lesser extent). The third factor (the “dietary n−3 PUFA” factor) comprised mainly positive loadings of polyunsaturated FAs (PUFAs; PUFA, polyunsaturated fatty acid).
The fatty acid–factor loadings of the 3 major principal component factors at age 70 y

<table>
<thead>
<tr>
<th>Fatty acid</th>
<th>Factor 1: low-LA factor</th>
<th>Factor 2: dietary SFA factor</th>
<th>Factor 3: n-3 PUFA factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>16:0</td>
<td>0.56</td>
<td>0.42</td>
<td>0.45</td>
</tr>
<tr>
<td>16:1</td>
<td>0.90</td>
<td>-0.13</td>
<td>-0.02</td>
</tr>
<tr>
<td>18:0</td>
<td>-0.14</td>
<td>-0.06</td>
<td>0.93</td>
</tr>
<tr>
<td>18:1</td>
<td>0.72</td>
<td>0.09</td>
<td>0.17</td>
</tr>
<tr>
<td>18:2n-6</td>
<td>-0.90</td>
<td>-0.33</td>
<td>-0.21</td>
</tr>
<tr>
<td>18:3n-6</td>
<td>0.73</td>
<td>-0.25</td>
<td>-0.05</td>
</tr>
<tr>
<td>18:3n-3</td>
<td>0.09</td>
<td>-0.16</td>
<td>0.13</td>
</tr>
<tr>
<td>20:3n-6</td>
<td>0.52</td>
<td>-0.44</td>
<td>0.15</td>
</tr>
<tr>
<td>20:4n-6</td>
<td>0.35</td>
<td>0.44</td>
<td>-0.10</td>
</tr>
<tr>
<td>20:5n-3</td>
<td>0.31</td>
<td>0.67</td>
<td>0.12</td>
</tr>
<tr>
<td>22:6n-3</td>
<td>0.04</td>
<td>0.65</td>
<td>0.04</td>
</tr>
<tr>
<td>Δ9-16</td>
<td>0.84</td>
<td>-0.27</td>
<td>-0.15</td>
</tr>
<tr>
<td>Δ9-18</td>
<td>0.81</td>
<td>-0.17</td>
<td>0.009</td>
</tr>
<tr>
<td>D6D</td>
<td>0.52</td>
<td>0.10</td>
<td>-0.77</td>
</tr>
<tr>
<td>D5D</td>
<td>-0.16</td>
<td>0.77</td>
<td>-0.22</td>
</tr>
<tr>
<td>Even value</td>
<td>5.17</td>
<td>2.39</td>
<td>1.90</td>
</tr>
<tr>
<td>Total variance (%)</td>
<td>38</td>
<td>18</td>
<td>14</td>
</tr>
</tbody>
</table>

Factor loadings that contribute to defining each factor.

Factor scores at age 50 y and risk of MetS

In a cross-sectional analysis, all 3 factor scores were significantly associated with MetS, independent of one another at age 50 y (Table 4). The unadjusted odds ratios (and 95% CIs) of having MetS were 1.55 (1.38, 1.77), 1.35 (1.19, 1.53), and 0.56 (0.48, 0.64) (P < 0.0001 for all) for factors 1, 2, and 3, respectively. The relation between the individual factor scores and MetS was independent of physical activity, smoking habit, and BMI.

In the prospective analysis, factors 1 and 3 significantly predicted the development of MetS over 20 y. These relations were also independent of the activities of the other desaturases (data not shown), smoking habit, physical activity, and BMI. BMI attenuated the odds ratios the most, but this was expected because BMI was one component included to identify the MetS (Table 5).

Fatty acid factor scores and the metabolic syndrome

When factor scores were investigated in relation to MetS, significantly higher loading scores were observed for those who had MetS for factors 1 and 2 at age 50 y and for factor 1 at age 70 y. Factor 3 was significantly lower in subjects with MetS at age 50 y. The scores of factors 2 and 3 at age 70 y did not differ significantly between subjects with or without MetS and were therefore not explored further in this study (Table 4).

Mean (±SEM) scores for factor 1 at ages 50 and 70 y in relation to the number of MetS criteria that were met in the subjects of the population are shown in Figure 1 and Figure 2. The mean score for the low-LA factor increased with 0.23 and 0.20 for each added MetS risk factor at ages 50 and 70 y, respectively (P < 0.0001).

Figure 1. Mean (±SEM) factor scores for factor 1 (low–linoleic acid factor) in subjects aged 50 y who had 0, 1, 2, 3, 4, or 5 of the risk factors for the metabolic syndrome (MetS) (mean score for factor 1 = 0.76 ± 0.02 SEM). The mean score for factor 1 at age 70 y increased with 0.22 (P < 0.0001 SEM).
Cross-sectional analysis at age 50 y

Multivariate logistic regression analysis

TABLE 5

The odds ratios (and 95% CIs) of factors 1, 2, and 3 associated with having and developing the metabolic syndrome determined by univariate and multivariate logistic regression analysis

DISCUSSION

We showed in this study that the generated FA factors, which represent dietary fat quality and endogenous FA metabolism, may be important in the development of MetS. A high factor 1 (low LA) and a low factor 3 (n–3 PUFA) significantly predicted the development of MetS over 20 y, independent of lifestyle factors. This finding suggests that changes in FA composition and desaturase activities appear long before the onset of MetS. However, the results of this study do not give us any clues regarding what might cause the changes in FA composition and desaturase activities, because dietary fat intake, genetic predisposition, and other factors (eg, hormonal factors) may influence this process.

The prevalence of MetS is increasing throughout the world because of the growing obesity epidemic (18). Insulin resistance often accompanies obesity, and this predisposes to MetS. It was previously shown that FA composition influences the development of insulin resistance (3), and, in a recent study, we showed that FA composition and a lower D5D activity predict the development of MetS over 20 y (19). In the present study we found cross-sectional FA composition to be significantly different between subjects with or without MetS. The proportions of 16:0, 16:1, 18:1n–9, 18:3n–6, 20:3n–6, Δ9–16, and Δ6D were significantly higher at the same time as 18:2n–6 and D5D were significantly lower in subjects with MetS at the ages of 50 and 70 y. This finding confirms the findings of previous studies that investigated the association between FA composition and metabolic disease (10).

We also found that all 3 FA factors at age 50 y and factor 1 (low LA) at age 70 y were significantly different between those with or without MetS. The relations between each FA factor and MetS at age 50 y were independent of lifestyle factors such as smoking habit, physical activity, and BMI. This might indicate that the quality of dietary fat, independent of the amount of fat (BMI is a marker of unhealthy diet and general overweight), is important in the development of MetS. It is known that physical inactivity (20) and smoking (21) can induce insulin resistance, yet the relations between FA factors and MetS were independent of these factors. The FA factors that we defined (Tables 2 and 3) were all characterized by specific FA patterns that we interpreted as partly a consequence of dietary fat quality. The most powerful FA factor (factor 1) that emerged from the factor analysis had a FA pattern that is often associated with metabolic disease and a high intake of SFAs simultaneous with a lower intake of LA (3). We called this the low-LA factor because the negative influence of LA was dominant. The same pattern emerged at both ages 50 and

FIGURE 2. Mean (±SEM) factor scores for factor 1 (low–linoleic acid factor) in subjects aged 70 y who had 0, 1, 2, 3, 4, or 5 of the risk factors for the metabolic syndrome (MetS): fasting glucose ≥6.1 mmol/L, systolic blood pressure ≥130 mm Hg or diastolic blood pressure ≥85 mm Hg or antihypertensive medication use, triacylglycerol concentration ≥1.69 mmol/L, HDL-cholesterol concentration <1.04 mmol/L, or waist circumference >102 cm. Factor 1 comprised mainly positive loadings from 16:1, 18:1n–9, 18:3n–6, the ratio of 16:1n–7 to 16:0, and Δ5-desaturase activity and an inverse loading of 18:2n–6. P for trend < 0.0001 (β coefficient = 0.20) derived from linear regression analysis.

TABLE 5

The odds ratios (and 95% CIs) of factors 1, 2, and 3 associated with having and developing the metabolic syndrome determined by univariate and multivariate logistic regression analysis

\[
\begin{array}{ccc}
\text{Factor 1: low-LA factor} & \text{Factor 2: dietary SFA factor} & \text{Factor 3: n–3 PUFA factor} \\
\hline
\text{Cross-sectional analysis at age 50 y} & & \\
\text{Crude (n = 2009)} & 1.55 (1.38, 1.76) & 1.35 (1.19, 1.53) & 0.56 (0.48, 0.64) \\
\text{Adjusted for BMI (n = 2009)} & 1.21 (1.10, 1.40) & 1.37 (1.18, 1.59) & 0.64 (0.55, 0.75) \\
\text{Adjusted for model 1 (n = 1838)} & 1.22 (1.05, 1.42) & 1.33 (1.14, 1.56) & 0.64 (0.55, 0.75) \\
\text{Prospective analysis between ages 50 and 70} & & & \\
\text{Crude (n = 946)} & 1.51 (1.28, 1.79) & 1.09 (0.93, 1.29) & 0.76 (0.64, 0.90) \\
\text{Adjusted for BMI (n = 946)} & 1.26 (1.05, 1.51) & 1.12 (0.93, 1.33) & 0.80 (0.67, 0.96) \\
\text{Adjusted for model 1 (n = 880)} & 1.16 (0.96, 1.40) & 1.13 (0.94, 1.37) & 0.78 (0.64, 0.94) \\
\text{Adjusted for model 2 (n = 880)} & 1.40 (1.17, 1.66) & 1.11 (0.94, 1.32) & 0.74 (0.62, 0.89) \\
\end{array}
\]

1 LA, linoleic acid; SFA, saturated fatty acid; PUFA, polyunsaturated fatty acid.
2 \( P < 0.0001. \)
3 \( P < 0.05. \)
4 Adjusted for BMI, smoking habits, and physical activity.
5 Subjects with the metabolic syndrome at age 50 y were excluded.
6 Adjusted for smoking habits and physical activity.
7 \( P < 0.001. \)
70 y. We also found that the mean score for the low-LA factor, at both ages 50 and 70 y, increased as the number of MetS criteria met increased, which also indicates an association between fat quality and MetS (Figures 1 and 2). A higher mean score for factor 2, the dietary SFA factor, at age 50 y was associated with a higher associated risk of having MetS. The associations between the low-LA and dietary SFA factors at age 50 y and MetS support the findings of previous studies about dietary fat quality and disease risk. Epidemiologic studies have shown that a diet high in SFAs decreases insulin sensitivity, whereas a diet high in unsaturated fats improves insulin sensitivity (22). The KANWU study showed that substituting SFA for MUFA improves insulin sensitivity (11). (KANWU refers to the location of the study centers: Kuopio, Aarhus, Naples, Wollongong, and Uppsala.) Substituting unsaturated fat or carbohydrates for SFA induces a similar FA pattern, as was observed in persons with MetS (3). Such a pattern was previously shown to predict cardiovascular disease (15, 23, 24) and type 2 diabetes (25–27).

FAs of the n-3 family are generally regarded as being protective against cardiovascular disease (28, 29), which is supported by our results, ie, a higher n-3 PUFA factor (factor 3) score was negatively associated with MetS. D5D activity in skeletal muscle membranes was previously shown to be associated with better insulin sensitivity (30, 31), and previous studies in the ULSAM cohort showed that low D5D activity independently predicts MI (15) and that D5D activity is negatively associated with plasminogen activator inhibitor 1 (32). The positive loading from D9-18 in factor 3 (Table 2) might seem surprising, because high SCD-1 activity is associated with insulin resistance. However, the proportion of 18:1n-9 in serum CEAs might reflect dietary intake more so than endogenous FA synthesis, which may be compatible with a healthy diet (2).

The association between an altered FA composition and metabolic disease was established previously (3, 10), but the role of desaturases is not as clear. We included the estimated desaturase activities in the factor analysis because we believe that it is important to consider desaturase activities in the development of metabolic disease. High SCD and D6D activities and a low D5D activity are generally associated with insulin resistant states (3). Desaturases are crucial for general body and FA metabolism. These systems are intricately regulated, and genetic, hormonal, and environmental factors influence the expression and action of desaturases (33). SCD synthesizes MUFAs from SFAs, whereas D5D and D6D catalyze the synthesis of long-chain n-6 and n-3 PUFAs. MUFA synthesis is required for the FA composition of membrane phospholipids, adipose tissue triacylglycerol, and CEAs (33, 34). PUFAs are incorporated into membrane phospholipids but are also needed for eicosanoid signaling and regulation of gene expression (33). It has been suggested that FA composition affects insulin action through its influence on membrane fluidity (31), and desaturases are central in maintaining membrane fluidity. Thus, a diet high in SFAs and low in PUFAs may influence many functions in the cell by reducing the amount of unsaturated FAs in membranes and reducing the availability of substrate for eicosanoid synthesis, which mediates local reactions such as inflammation and hemostasis (33).

We found some differences concerning the relations between the FA factors and MetS at ages 50 and 70 y. These discrepancies may have resulted because of differences in fat intake (35), differences in enzyme activity, or limited power in the analyses, especially at age 70 y. In a previous study of the ULSAM cohort, Öhrvall et al (35) found that the CE FA composition remained fairly stable over time and that the methods used for analyzing the FA data were comparable. They concluded that changes in both diet and body weight were relatively small over the course of 20 y.

This study had both strengths and limitations. One limitation was that it was an observational study; therefore, the causality of the relations was unknown. Another limitation was that the study population consisted of only men; therefore, our results need to be verified in women. A strength of the study was that it defined FA factors to be used as a tool to simplify future studies of dietary fat quality and the influence of endogenous metabolism in relation to the development of disease.

In conclusion, this study shows the importance of dietary fat quality, as evaluated by FA factors generated in principal component analysis, in the development of MetS. The main findings of this study agree well with current dietary recommendations to increase the intake of PUFAs and to restrict the intake of SFAs (36).

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