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Fatty acid composition of serum lipids predicts the development of the metabolic syndrome in men

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Abstract *Aims/hypothesis:* Types of dietary fat have been related to components of the metabolic syndrome. Serum fatty acid composition mainly reflects dietary fat intake, but also endogenous fatty acid synthesis catalysed by Δ-desaturases. It is not known whether alterations of fatty acid composition or desaturase activities predict metabolic syndrome. *Materials and methods:* We prospectively evaluated fatty acid composition in serum cholesteryl esters and estimated desaturase activities in 1,558 50-year-old men taking part in a population-based cohort study. The follow-up time was 20 years. Stearoyl-CoA desaturase (SCD-1), Δ6 (D6D) and Δ5 (D5D) desaturases were estimated as precursor to fatty acid ratios. *Results:* High activity of estimated SCD-1 (odds ratio=1.29, $p<0.05$) and D6D (odds ratio=1.35, $p<0.05$), as well as low estimated D5D activity (odds ratio=0.71, $p<0.001$) predicted the development of metabolic syndrome (as defined by the National Cholesterol Education Program). The predictive value of D5D activity was independent of lifestyle factors (smoking, BMI and physical activity), whereas the risk associated with higher SCD-1 and D6D activities was mainly explained by obesity. Among those developing metabolic syndrome (119 out of 706) during follow-up, the proportions of fatty acids 14:0, 16:0, 16:1 (*n*−7), 18:1 (*n*−9), 18:3 (*n*−6) and 20:3 (*n*−6) were increased at baseline, while 18:2 (*n*−6) was decreased ($p<0.05$ for all). *Conclusions/interpretation:* Serum fatty acid composition predicts the long-term development of the metabolic syndrome, and D5D activity may be particularly important in this process. Our results suggest a role of dietary fat quality in the development of metabolic syndrome, but the possibility that altered fatty acid composition, partly secondary to genetic or hormonal factors, should also be considered.

Keywords Δ-desaturase · Δ5-desaturase · Dietary fat · Fatty acid composition · Metabolic syndrome · Stearoyl-CoA desaturase

Abbreviations D5D: Δ5-desaturase · D6D: Δ6-desaturase · OR: odds ratio · SCD-1: stearoyl CoA desaturase-1 · sCE: serum cholesteryl ester · ULSAM: Uppsala Longitudinal Study of Adult Men

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Introduction

The metabolic syndrome is a cluster of risk factors including abdominal obesity, hypertension, insulin resistance and dyslipidaemia. Patients with metabolic syndrome are at increased risk of type 2 diabetes and cardiovascular disease [1].

Several aetiological factors are involved in the development of metabolic syndrome, in which obesity and insulin resistance may be the most central factors [1]. Diet and physical inactivity are lifestyle factors promoting obesity and thus the metabolic syndrome. Dietary fat quality may affect insulin sensitivity [2] and intervention studies have shown that the plasma fatty acid pattern changes after substituting saturated fatty acids for monounsaturated fatty acids [3], resulting in better insulin sensitivity [2]. Interestingly, a diet rich in saturated fatty acids induces the same serum fatty acid pattern as that seen in individuals with signs of metabolic syndrome [3].

It is known that the fatty acid composition in serum lipid esters mirrors the dietary fatty acid composition during the last 6–8 weeks [4–7]. The serum fatty acid pattern is also dependent on endogenous synthesis of fatty acids, which in turn is also influenced by genetic variation and intrauterine programming [3]. Desaturases are involved in endogenous fatty acid synthesis and Δ9 desaturase or stearoyl CoA desaturase (SCD), Δ6 desaturase (D6D) and Δ5 desaturase (D5D) introduce a double bond in specific positions of long-chain fatty acids. SCD synthesises monounsaturated fatty acids from saturated fatty acids, while D5D and D6D catalyse the synthesis of long-chain *n*−6 and *n*−3 polyunsaturated fatty acids. Monounsaturated fatty acid synthesis is required for the fatty acid composition of membrane phospholipids, adipose tissue triglycerides, and cholesteryl esters [8, 9]. Polyunsaturated fatty acids are incorporated into membrane phospholipids, but are also needed for eicosanoid signalling and regulation of gene expression [8]. The serum fatty acid composition has been shown to predict the risk of diabetes and cardiovascular disease [10, 11] and recently it was closely related to components of the metabolic syndrome in a cross-sectional study [12]. Prospective studies are, however, needed to investigate the role of fatty acid composition in the development of metabolic syndrome. In addition, the desaturase activities per se may be more important predictors of metabolic disorders than the individual fatty acids [3]. Studies on SCD-1-deficient mice have suggested a key role of this enzyme in obesity-related metabolic diseases [9, 13], and D5D activity has been positively associated with insulin action in Pima Indians [14]. The activities of desaturase can be estimated using fatty acid product-to-precursor ratios [3, 8]. The aim of the present study was to examine the predictive role of estimated desaturase activities as well as of individual fatty acids in serum cholesteryl esters (sCE) in the development of metabolic syndrome over a 20-year period.

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. All men born between 1920 and 1924 and living in Uppsala were invited to participate. The participants were examined at baseline at age 50 years and reinvestigated at age 70. At baseline, 2,841 men were invited and 82% (2,322) agreed to participate. At age 70, 1,681 men were invited to participate and 73% (1,221) participated. To define our study population, we excluded those participants who were hypertensive (supine diastolic BP ≥95 mmHg), were taking BP medication, had diabetes (blood glucose ≥6.7 mmol/l [15], *K*-value ≤0.9 or antidiabetic therapy) or were currently taking medication for hyperlipidaemia at the age of 50. (See also http://www.pubcare.uu.se/ULSAM/.) After the exclusions, 1,558 men remained for analyses at baseline. The definitions used for hypertension and diabetes prevalence are old, but they were used because the measurements were performed in the early 1970s. Using these definitions for the exclusions will not affect the results of this study. In the prospective analyses we excluded those who already had metabolic syndrome at age 50 and participated in the 70-year investigation (see flowchart in Fig. 1). The study was approved by the ethics committee at Uppsala University and all participants had given their informed consent to participate.

Investigations at 50 years

All investigations were performed under standardised conditions and have been described in detail previously

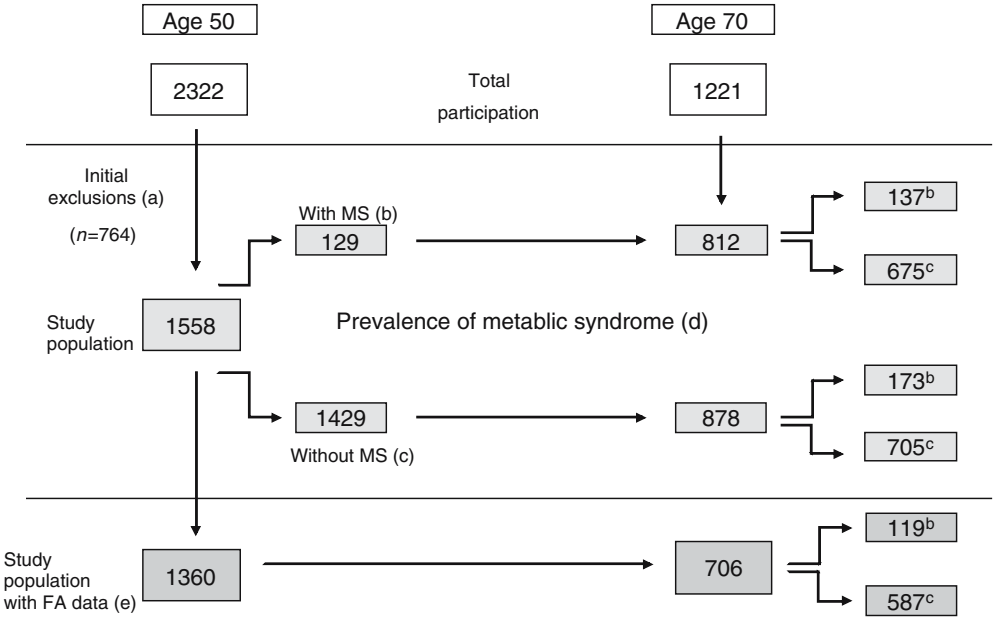

Fig. 1 Flowchart. **a** Initial exclusions are men who had diabetes or hypertension or were taking blood pressure or lipid lowering drugs (*n*=764). **b** Number of subjects with the metabolic syndrome at the ages of 50 and 70. **c** Number of subjects without the metabolic syndrome at the ages of 50 and 70. **d** Calculation of the prevalence of the metabolic syndrome in the present study. **e** Number of subjects with and without the metabolic syndrome who had complete fatty acid data. Fatty acid composition and desaturase activities were calculated for these subjects

[16, 17]. The investigations included a medical questionnaire and interview, as well as blood sampling, anthropometric measurements and BP. Supine BP was recorded in the recumbent position with a mercury manometer (Kifa Ercameter, wall model). Blood samples were drawn after an overnight fast, and triglycerides, lipoproteins, serum cholesterol, serum cholesteryl ester fatty acids, blood glucose and serum insulin were measured. BMI was calculated as weight (kg) divided by height (m) squared. Blood glucose was measured by spectrophotometer using the glucose oxidase method. Serum insulin concentrations were determined with the Phadebas Insulin Test (Pharmacia, Uppsala, Sweden). Fatty acid composition was analysed as previously described [18]. Serum was extracted with a hexane-isopropanol solution and cholesteryl esters (only lipid esters that were measured at baseline) were separated from the extract by thin-layer chromatography before inter-esterification with acidic methanol was performed. Free cholesterol that had been liberated in the reaction was removed by aluminium oxide to avoid contamination of the column. The composition of methylated fatty acids was determined by gas chromatography (25 m NB-351 silica capillary column) with a flame ionisation detector and helium as carrier gas. Every 25th sample was a serum control pool. The CV between successive gas chromatography runs was 0.2–5%. The relative amount of fatty acid was expressed as a percentage of the total amount of fatty acids. The number of subjects with fatty acid data at baseline was 1,360. The total number of subjects with fatty acid data is not equal to the total number of study subjects since some of the samples were not available for analyses at the age of 50 (see flowchart in Fig. 1).

Investigations at 70 years

The measurements at 70 years were performed in a similar manner as at age 50 and are described in detail elsewhere [19, 20]. Triglycerides, lipoproteins, serum cholesterol, sCE fatty acids, blood glucose and serum insulin concentrations were measured, as well as anthropometry and BP. A medical questionnaire and interview were also performed.

Definition of the metabolic syndrome

There are several definitions of metabolic syndrome available and in the present study we used the definition of the National Cholesterol Education Program (Adult Treatment Panel III), since it is the most recently suggested and practical for use in the clinical setting [1]. A patient is classified as having the metabolic syndrome when three or more of the following risk determinants are present: fasting glucose ≥6.1 mmol/l, systolic BP ≥130 mmHg or diastolic BP ≥85 mmHg, triglyceride level ≥1.69 mmol/l, HDL-cholesterol concentration <1.04 mmol/l, or waist circumference >102 cm. Waist circumference was only recorded in only 325 of the 50-year-old men. Therefore we used a BMI cut-off (29.2 kg/m^2) that corresponded to a waist circumference of 102 cm using linear regression analysis (BMI=0.2863×102 [cm]-0.034). This was derived from subjects with data on both BMI and waist circumference. Among the 70-year-old men, waist circumference >102 cm was used to define metabolic syndrome.

Estimation of desaturase activity

The desaturase activity was estimated as the product:precursor ratio of individual fatty acids in sCEs according to the following: SCD−1=(16:1[*n*−7]/16:0), D6D=(18:3[*n*−6]/18:2[*n*−6]), D5D=(20:4[*n*−6]/20:3[*n*−6]).

Statistical analysis

The statistical analyses were performed using the software package STATA (version 6.0; STATA, College Station, TX, USA). The normal distribution of continuous variables was examined with the Shapiro–Wilk test. Variables non-normally distributed (W<0.95) were log-transformed. Descriptive results are presented as mean±SD unless otherwise indicated. Student's t-test was used to test differences in means between desaturases and fatty acids, as well as baseline characteristics, in individuals with and without the metabolic syndrome. Logistic regression analysis was carried out to estimate the risk of having metabolic syndrome at the age of 70 in relation to estimated desaturase activities at 50 years. Standardised (SD=1.0) odds ratios (OR) were calculated. Univariate and multivariate logistic regression analysis was carried out. The following variables were included in the multivariate logistic regression models: (1) BMI+smoking behaviour; (2) smoking behaviour+physical activity; and (3) BMI+smoking behaviour+physical activity. Smoking status was considered a categorical variable (non-smoker=0, smoker=1 and ex-smoker=2 at 50 years) and (smoker=1 and non-smoker=0 at 70 years). Physical activity levels were graded from 1 (lowest) to 4 (highest). Values of p<0.05 were considered significant.

Results

Baseline metabolic characteristics

The baseline metabolic characteristics among the 50-year-old men with and without the metabolic syndrome were as described in Table 1. As expected, most of the characteristics associated with metabolic syndrome were significantly higher among those who 20 years later developed metabolic syndrome.

Prevalence of the metabolic syndrome

The prevalence of the metabolic syndrome at baseline was 8.3% (129/1,558) after the initial exclusions. This figure might seem low but, as previously described, we excluded

Table 1 Baseline characteristics of those members of the study population who, after initial exclusions (see flowchart in Fig. 1), had or had not developed the metabolic syndrome 20 years later

Variable	Subjects without metabolic syndrome	Subjects with metabolic syndrome	Difference
	Mean±SD	Mean±SD	*p*-value[a]
Systolic BP (mmHg)	125.6±11.9	128.5±11.5	<0.05
Diastolic BP (mmHg)	78.5±7.0	80.0±6.0	<0.05
Fasting blood glucose (mmol/l)	4.9±0.5	5.0±0.8	<0.001
Fasting serum insulin (μU/ml)	10.0±1.0	11.5±1.0	<0.05
BMI (kg/m^2)	23.9±2.4	25.6±2.5	<0.0001
Waist circumference (cm)	84.4±6.7	88.2±7.2	<0.05
HDL-cholesterol (mmol/l)	1.5±0.4	1.3±0.3	<0.0001
Serum triglycerides (mmol/l)	1.5±0.6	1.7±0.5	<0.0001
HOMA insulin resistance index	2.4±1.2	3.0±1.8	<0.001

Those having metabolic syndrome at age 50 were excluded from the analysis
HOMA homeostasis model assessment
[a]$p<0.05$ was considered significant

many individuals who could have fulfilled the criteria of metabolic syndrome. At the age of 70 metabolic syndrome was more common, and when we excluded those having the syndrome at 50 the prevalence was 16.9% (137/812). The prevalence was 19.8% (173/874), when the entire 70-year-old-population was considered (see flowchart in Fig. 1).

Baseline fatty acid profile predicts the metabolic syndrome

The fatty acid profile in sCE at age 50 predicted the development of metabolic syndrome 20 years later. The relative amounts of the following fatty acids in sCE were significantly higher in those developing metabolic syndrome: 14:0, 16:0, 16:1 (*n*−7), 18:1(*n*−9), 18:3 (*n*−6) and 20:3 (*n*−6) (all $p<0.05$). Linoleic acid (18:2 *n*−6) was significantly ($p<0.05$) higher among those without the metabolic syndrome at age 70, but the levels of 20:4 (*n*−6), 20:5 (*n*−3) and 22:6 (*n*−3) did not differ between the two groups (Table 2 and flowchart, Fig. 1e).

Desaturase activity and the prediction of metabolic syndrome

The estimated serum desaturase activities in men who developed metabolic syndrome and those who did not are depicted in Table 2. The ratio was significantly higher for SCD-1 and D6D ($p=0.02$ and $p=0.004$, respectively) and lower for D5D activity ($p=0.001$) in those who developed metabolic syndrome during follow-up.

Table 2 Difference in relative amount of fatty acids and desaturase activities in serum lipids at the age of 50 in men who had (*n*=119) or had not (*n*=587) developed metabolic syndrome at age 70

Fatty acid (% of total fatty acids) and fatty acid ratio	Subjects without metabolic syndrome	Subjects with metabolic syndrome	Difference
	Mean±SD	Mean±SD	*p* value[a]
14:0 (myristic)	1.09±0.24	1.15±0.23	<0.05
16:0 (palmitic)	11.4±0.93	11.7±0.95	<0.05
16:1 *n*−7 (palmitoleic)	3.5±1.1	3.8±1.1	<0.05
18:0 (stearic)	1.14±0.3	1.17±0.3	0.34
18:1 *n*−9 (oleic)	18.9±2.5	19.4±2.2	<0.05
18:2 *n*−6 (linoleic)	55.4±4.7	54.0±4.4	<0.05
18:3 *n*−6 (γ-linolenic)	0.66±0.16	0.73±0.33	<0.05
18:3 *n*−3 (α-linolenic)	0.66±0.16	0.67±0.19	0.27
20:3 *n*−6 (dihomo-γ-linolenic)	0.54±0.13	0.60±0.15	<0.0001
20:4 *n*−6 (arachidonic)	4.74±0.94	4.79±1.0	0.6
20:5 *n*−3 (eicosapentaenoic)	1.30±0.57	1.38±0.74	0.28
22:6 *n*−3 (docosahexaenoic)	0.70±0.2	0.69±0.2	0.31
Δ9-16 (16:1 [*n*−7]/16:0)	0.31±0.09	0.33±0.09	<0.05
Δ6 (18:3 [*n*−6]/18:2 [*n*−6])	$0.012\pm6\times10^{-3}$	$0.014\pm7\times10^{-3}$	<0.05
Δ5 (20:4 [*n*−6]/20:3 [*n*−6])	9.0±2.1	8.3±2.1	<0.001

Those having the metabolic syndrome at the age of 50 were excluded from the analysis
[a]$p<0.05$ was considered significant

Table 3 Results of logistic regression analysis of the effect of desaturase activities at age 50 on classification as having or not having metabolic syndrome at age 70

Covariate	SCD-1[a] OR (95%CI)	D6D[a] OR (95%CI)	D5D[a] OR (95%CI)
Univariate analysis			
Crude (*n*=706)	1.29 (1.0, 1.60)[b]	1.35 (1.10, 1.65)[b]	0.71 (0.57, 0.87)[c]
Multivariate analysis			
BMI (*n*=706)	1.17 (0.93, 1.46)[NS]	1.23 (1.0, 1.52)[NS]	0.77 (0.62, 0.96)[b]
Physical activity (*n*=654)	1.16 (0.92, 1.46)[NS]	1.25 (1.0, 0.56)[b]	0.70 (0.56, 0.88)[b]
Smoking (*n*=706)	1.30 (1.0, 1.60)[b]	1.36 (1.10, 1.67)[b]	0.71 (0.57, 0.87)[b]
BMI+smoking habit (*n*=706)	1.17 (0.94, 1.47)[NS]	1.24 (1.0, 1.53)[b]	0.77 (0.62, 0.96)[b]
Smoking habits+physical activity (*n*=654)	1.16 (0.92, 1.47)[NS]	1.26 (1.0, 1.57)[b]	0.70 (0.56, 0.88)[b]
BMI+smoking habit+physical activity (*n*=654)	1.07 (0.84, 1.36)[NS]	1.16 (0.93, 1.46)[NS]	0.75 (0.60, 0.96)[b]

Those having metabolic syndrome at age 50 were excluded from the analysis
OR odds ratio; *NS*, not significant
[a]Standardised desaturase ratios were used in the analysis
[b]$p<0.05$
[c]$p<0.001$

In the logistic regression models (Table 3), in which standardised desaturase activity ratios were used, the relationships followed a pattern similar pattern to that when the *t*-test was used (Table 2). The risk of having metabolic syndrome at age 70 (men with metabolic syndrome at 50 years were excluded from the analysis) was increased at higher levels of estimated SCD-1 (OR=1.29, $p<0.05$) and D6D (OR=1.35, $p<0.05$) desaturase activities at 50 years of age, whereas it decreased with higher levels of D5D (OR=0.71, $p<0.0001$) at 50. Thus, for each SD increase in estimated levels of SCD-1 and D6D activity, there was an increase of roughly 30% in the risk of developing metabolic syndrome over 20 years. For D5D the situation was the opposite, with a reduction in the risk of 30% over the same period. When adjustment for several confounders were made, the relationship between estimated SCD-1 activity and the risk of having metabolic syndrome 20 years later disappeared, although the relationship was independent of smoking behaviour (OR=1.30, $p<0.05$). The relationship between D5D and metabolic syndrome remained after adjustment for all confounders, either singly or in combination. This relationship was also independent of the estimated activity of D6D and SCD-1. The relationship between D6D and metabolic syndrome remained after most adjustments, but BMI alone or in combination with smoking behaviour and physical activity removed the relationship.

Discussion

The results of the present study add new information about altered fatty acid metabolism as a predictor of metabolic syndrome.

We show that serum fatty acid composition was, already at baseline, significantly different in men who developed metabolic syndrome compared with those who did not during the 20 years of follow-up. These results are in line with previous findings from the ULSAM cohort regarding serum fatty acid profile and the risk of developing cardiovascular disease [21, 22] and type 2 diabetes [23]. The fatty acid composition in individuals with insulin resistance and metabolic syndrome is typically characterised by high levels of saturated fatty acids such as 16:0 and low levels of polyunsaturated fatty acids (18:2, *n*−6), and a proportionally higher level of palmitoleic (16:1, *n*−7) and dihomo-γ-linolenic (20:3, *n*−6) acids [3, 24, 25]. This pattern was observed in the subjects with metabolic syndrome in this study. In line with this, high serum proportions of linoleic (18:2 *n*−6) acid decreased the risk of type 2 diabetes in middle-aged men over a period of 4 years [26]. It was also recently reported that a higher proportion of saturated fatty acids (16:0+18:0) was prospectively and positively associated with an increased risk of cardiovascular disease [10] and type 2 diabetes [11].

Few studies have investigated estimated desaturase activities as predictors of metabolic diseases. Cross-sectionally, insulin-resistant states have often been associated with high activity of SCD-1 and D6D and low activity of D5D [3]. Low estimated D5D activity significantly predicted the development of metabolic syndrome in the present study, independently of lifestyle factors (smoking, physical activity and BMI) assessed at baseline, as well as the estimated activity of SCD-1 and D6D. Previous studies have reported decreased estimated D5D activity as an independent risk factor for myocardial infarction [24], and Byberg and colleagues found estimated D5D activity to be negatively associated with PAI-1 activity [27]. Our data might indicate that low estimated D5D activity is an early sign of the risk of developing metabolic syndrome, which 20 years later results in manifest metabolic syndrome. In the logistic regression analysis, higher estimated activity of SCD-1 and D6D increased the risk of developing metabolic syndrome over 20 years. The relationship between D6D and metabolic syndrome was independent of smoking behaviour, physical activity, and BMI in combination with smoking, whereas the effect of estimated SCD-1 activity was only independent of smoking. This suggests that the effect of

estimated D6D and D5D activity on the development of metabolic syndrome is more or less independent of lifestyle factors, whereas the effect of the SCD-1 ratio may be mediated via life style factors such as physical inactivity and other factors that promote obesity. Although the association with estimated D5D activity was independent of confounders, there may be other confounders that we have not accounted for, such as dietary factors (i.e. total carbohydrate and type of carbohydrate), proinflammatory markers and adiponectin concentrations.

While this and other studies have shown that increased estimated SCD-1 activity is related to metabolic disorders [3, 13], it should be kept in mind that such a relationship may reflect compensatory up-regulation of SCD-1 to continuous intake of an unhealthy diet, e.g. a diet high in saturated fatty acids and low in polyunsaturated fatty acids, rather than a metabolically harmful effect of increased SCD-1 activity in itself. Our results support such a hypothesis, since the relationship between SCD-1 and metabolic syndrome was confounded by BMI, a marker of general overweight and an unhealthy diet, which is different from the abdominal adiposity that is included in the metabolic syndrome.

Notably, SCD-1 activity can also be estimated as the 18:1 ($n-9$):18:0 ratio. However, in our study the predictive value of this ratio was not significant (data not shown), which may be explained by a much higher dietary proportion of 18:1 compared with 16:1, which is compatible with a healthy diet. In the present cohort dietary records were only recorded at the age of 70. In this investigation the mean intake of 18:1 was 16 times higher than that of 16:1 (19.7 vs. 1.3 g/day). We believe that the intake of dietary fatty acids was principally the same at the ages of 50 and 70. This is analogous to findings in another study of about 1,000 individuals at the age of 50 (M. Öhrvall and B. Vessby, unpublished data). Another study conducted in the present ULSAM population [28] showed that the fatty acid composition of cholesteryl esters remained fairly stable in relative amounts over time (50 to >70 years). This suggests that the fat quality was essentially the same over the same time.

It is known that the type of fat in the diet is important for the fatty acid composition of body tissues, as well as endogenous fatty acid metabolism, in which desaturases play an important part. Endogenous metabolism strives to desaturate and elongate dietary fatty acids since longer and more unsaturated fatty acids have more specific functions; for example, they maintain membrane fluidity and regulate the amount of eicosanoid precursors [8]. Fatty acid desaturation is dependent not only on the amount of dietary fatty acid but also on the quantity of other fatty acids present in body tissues, as well as enzyme activity [3]. Intervention studies have shown that a diet high in saturated fatty acids and low in polyunsaturated fatty acids induces the same fatty acid pattern as that linked with insulin resistance and metabolic syndrome [3, 21]. Moreover, polyunsaturated fatty acids downregulate the expression of SCD-1 and D6D [29], whereas saturated fatty acids and a fat-rich diet are associated with upregulated expression. Thus, the regulation of fatty acid composition is very complex. Genetic differences in fatty acid desaturases might also predispose to the metabolic syndrome. Recent studies show that mice lacking the SCD gene have improved glucose metabolism and are leaner than their wild-type littermates, and the genes involved in lipid synthesis are downregulated [9].

There are some limitations of this study. This is an observational study and therefore the causality of the relationships is unknown. The study population consisted only of men and therefore our results need to be verified in women. In another study we found that estimated SCD-1 activity was higher for women [30] , a finding which was also reported by another group [31]. However, in our other study, higher estimated SCD and D6D ratios and lower estimated D5D activity were associated with overweight both in men and women. Since direct measures of desaturase activities are very difficult to obtain in larger studies, we used the ratio between individual fatty acids, which also is a restriction. Conclusions about actual enzyme activity cannot be made, but estimated desaturase activities may be useful for understanding fatty acid desaturation patterns in metabolic syndrome.

In conclusion, this study shows that a changed serum lipid fatty acid composition and estimated desaturase activities predict metabolic syndrome over 20 years in middle-aged men. The risk of developing metabolic syndrome increased by 30% for each SD increase of SCD-1 and D6D activity, whereas the risk decreased equally for each SD increase in D5D activity. The results accord with previous data suggesting that altered fatty acid metabolism is associated with insulin resistance. The clinical relevance of these results requires further study, and it is too early to suggest that these alterations in fatty acid composition could be clinical predictors of the metabolic syndrome. We consider the alterations in fatty acid composition and desaturase activities in the present study as signs of disturbed fatty acid metabolism (probably secondary to dietary fat intake) that may be involved in the pathophysiology of metabolic syndrome. It is known that metabolic syndrome increases the risk of cardiovascular morbidity and mortality [1, 32], and our prospective data are of clinical importance and support the hypothesis that the type of dietary fat is a modifiable risk factor of cardiovascular disease.

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