Saturated Fat Intake and Insulin Resistance in Men With Coronary Artery Disease

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Background. **To determine whether there is an association between diet and plasma insulin concentration that is independent of obesity, we studied the relation of dietary composition and caloric intake to obesity and plasma insulin concentrations in 215 nondiabetic men aged 32–74 years with angiographically proven coronary artery disease.**

Methods and Results. **After adjusting for age, the intake of saturated fatty acids and cholesterol were positively correlated ($p<0.05$) with body mass index ($r=0.18$, $r=0.16$), waist-to-hip circumference ratio ($r=0.21$, $r=0.22$), and fasting insulin ($r=0.26$, $r=0.23$). Carbohydrate intake was negatively correlated with body mass index ($r=-0.21$), waist-to-hip ratio ($r=-0.21$), and fasting insulin ($r=-0.16$). Intake of monounsaturated fatty acids did not correlate significantly with body mass index or waist-to-hip circumference ratio but did correlate positively with fasting insulin ($r=0.24$). Intake of dietary calories was negatively correlated with body mass index ($r=-0.15$). In multivariate analysis, intake of saturated fatty acids was significantly related to elevated fasting insulin concentration independently of body mass index.**

Conclusions. **These cross-sectional findings in nondiabetic men with coronary artery disease suggest that increased consumption of saturated fatty acids is associated independently with higher fasting insulin concentrations. (*Circulation* 1991;84:2020–2027)**

Insulin resistance in the absence of overt diabetes may underlie several risk factors for coronary artery disease.[1,2] Hyperinsulinemia is a consequence of insulin resistance.[3] Even though the development of insulin resistance may be determined genetically,[4] its clinical manifestation may often require the presence of specific environmental factors.[5] Two environmental factors that promote the expression of insulin resistance are obesity[6–9] and physical inactivity.[9,10]

Diet was proposed as an environmental determinant of insulin sensitivity over 50 years ago,[11] but its role in the development of insulin resistance is less well established. Countries with higher intakes of fat and lower intakes of carbohydrate have a higher prevalence of diabetes, but such countries also have a higher prevalence of obesity.[12] Men who eat meat have been shown to have a higher prevalence and incidence of diabetes compared with vegetarian men independent of obesity and physical activity.[13,14] Increased consumption of butter is associated with higher glucose concentrations in Italian men and women.[15] Short-term clinical trials have shown that feeding a high-carbohydrate, low-fat diet to healthy and diabetic subjects improves insulin sensitivity.[11,16–20] It is possible that the specific composition of fatty acids in the diet may be related to insulin sensitivity. Kinsell et al[21] found that isocaloric substitution of a polyunsaturated fatty acid for a saturated-monounsaturated fat resulted in improved glucose levels in diabetic patients, and Houtsmuller et al[22] reported a beneficial effect on insulin status and glucose tolerance tests in obese diabetics on a diet rich in polyunsaturated fatty acids. Greenland Eskimos, who eat a high proportion of their fat as ω-3 fatty acids, have a lower prevalence of diabetes than Western Europeans[23] despite consuming a diet relatively high in total fat.[24]

The purpose of this cross-sectional study was to explore the relation of dietary composition to fasting plasma insulin concentration in nondiabetic men with established coronary artery disease. In addition, because recent cross-sectional studies suggest that dietary fat, and particularly saturated fatty acids, may play a role in the development of obesity,[25,26] we also studied the relation of saturated fatty acids to obesity.

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Methods

Study Population and Study Design

We selected 215 nondiabetic men out of 258 men with angiographically proven coronary artery disease who agreed to participate in a 4-year study of the effect of multiple risk factor intervention on the progression of coronary artery atherosclerosis. Subjects were recruited from four local hospitals where they were undergoing coronary angiography for suspected coronary artery disease. Angiography was performed using a research protocol if the subjects were 75 years old or younger, lived within a 6-hour driving radius of Stanford University, and were free from any other cardiac or noncardiac diseases that might severely limit life expectancy or ability to participate in the study. After angiography, if subjects had at least one coronary artery segment with lumen narrowing between 5% and 70% that had not been subjected to coronary artery bypass grafting or angioplasty, they were recruited into the study. For the purposes of this cross-sectional study, we excluded 37 of the 258 men entered into the clinical trial who had either a history of diabetes or fasting glucose concentration equal to or greater than 7.77 mmol/l (140 mg/dl). Six additional men were excluded from the current analysis because of incomplete data, leaving a sample of 215 men. This sample ranged in age from 32 to 74 years (mean±SD, 57.0±8.9).

Measurements

Four-day food records (Thursday through Sunday) were completed by each subject after receiving instruction from a research assistant trained in the use of a detailed, standardized protocol that included the use of food models, household measures, and a documentation checklist. Once completed, the records were reviewed with the subject for verification of amounts, preparation method, and restaurant or manufacturer information. The records were then analyzed using the code book and data base of the Nutrition Coding Center, Minneapolis, Minn. (version 9).[27]

To assess physical activity over the previous week and year, all subjects completed the Stanford Seven Day Physical Activity Recall questionnaire.[28] Subjects were asked if they exercised regularly over the previous year. They were asked to recall the number of minutes over the previous week spent engaged in moderate, hard, and very hard activities. Activities were expressed in terms of total kilocalories per kilogram per day—kilocalories per kilogram per day of moderate, hard, very hard, and hard plus very hard activity (1 kcal=4.2 kJ). They were also asked if they routinely made active life-style choices such as climbing stairs instead of taking an elevator or walking instead of driving a short distance. To evaluate cardiopulmonary fitness, all subjects underwent symptom-limited treadmill exercise testing by using a modified Naughton protocol. A smoking history was obtained to determine whether the person was a current or ex-smoker, to assess the number of cigarettes smoked per day, and to derive pack-years, defined as the number of packs smoked per day multiplied by the number of years of smoking.

Three indexes of obesity were obtained: body mass index (BMI), change in BMI since age 20 (ΔBMI), and waist-to-hip ratio (WHR). To obtain the BMI indexes, weight and height were measured with subjects wearing lightweight clothing or a hospital gown without shoes. Weight was measured to the nearest 0.1 kg using a balance scale. Height was measured to the nearest 0.5 cm with the patient standing erect, flat footed, and with the head in the Frankfort horizontal plane. BMI was calculated by dividing weight in kilograms by the square of the height in meters (kg/m^2). We created the ΔBMI variable by asking subjects to recall their weight at age 20 years. We assumed that height was constant since age 20, calculated BMI at age 20, and subtracted BMI at age 20 from BMI measured at baseline to yield ΔBMI. We measured waist and hip circumferences to calculate the WHR in a subset of 128 men. The waist was defined as the minimal circumference between the inferior border of the rib cage and the superior border of the iliac crests for those with a concave waist. For those with a convex waist, the waist was defined as midway between the inferior border of the rib cage and the superior border of the iliac crests. The hip was defined as the maximal circumference of the buttocks. The measurements were made with a flexible tape measure held horizontally and touching the skin without compressing the underlying tissue while the subject stood breathing normally. All measurements were made by a small group of trained personnel.

Plasma glucose and insulin concentrations were measured after an overnight fast and 1 hour after a 100-g oral glucose load. Glucose concentration was measured using the glucose oxidase method.[29] Insulin concentration was determined by radioimmunoassay.[30]

Statistical Analysis

We expressed calorie-contributing macronutrients as a percentage of total calories consumed (1 calorie equals 4.2 J). Cholesterol intake was analyzed as milligrams per 1,000 kcal. Adjusting nutrients for energy intake permits the study of associations of the qualitative composition of the diet with other variables.[31,32] Use of nutrient densities rather than absolute amounts reduces interindividual variation in nutrient intake that is due to differences in body size, physical activity, and metabolic efficiency.[31]

The relations between dietary, smoking, and exercise variables and measures of obesity, insulin, and glucose levels were assessed by age-adjusted Pearson correlation coefficients.[33] Probability values are for two-tailed significance. Partial correlation and multiple regression analyses were performed according to the procedure outlined in the SAS *User's Guide* (SAS Institute, Inc., Cary, N.C.). Given the number of tests in this exploratory data analysis, probability values of less than 0.05 should be interpreted with caution.

TABLE 1. Dietary Characteristics of 215 Nondiabetic Men With Coronary Artery Disease Aged 32–74 Years

Variable	Mean±SD	Range
Total fat* (% of total calories)	31.9±8.9	8.0–54.0
Saturated fatty acids (% of total calories)	10.0±3.9	2.2–22.1
Monounsaturated fatty acids (% of total calories)	12.0±4.0	2.2–23.2
Polyunsaturated fatty acids (% of total calories)	7.5±2.9	2.2–19.3
Cholesterol (mg/1,000 calories)	139±70	14–443
Carbohydrate (% of total calories)	45.7±9.9	18.0–70.0
Protein (% of total calories)	17.0±3.7	8.0–31.0
Alcohol (% of total calories)	5.4±6.5	0–28.0
Total calories (kcal)	2,075±584	638–3,739

*Total fat amount is greater than the sum of the individual fatty acids because of the presence of nonsaponifiable dietary lipids.
1 Calorie=4.2 J, 1 kcal=4.2 kJ.

Results

Tables 1 and 2 summarize the characteristics of the subjects with respect to measures of diet, obesity, insulin, glucose, smoking, and fitness. Thirty percent of subjects had never smoked, 56% were ex-smokers, and 14% were current smokers.

Correlation Analysis

Age-adjusted Pearson correlation coefficients of dietary variables and measures of obesity, insulin, and glucose are provided in Table 3. The most consistent statistically significant findings were 1) saturated fatty acid and cholesterol consumption correlated positively with all three indexes of obesity and with both measures of insulin, 2) carbohydrate consumption correlated negatively with all measures of obesity and with both measures of insulin, and 3) all measures of obesity were correlated positively with fasting insulin levels. Monounsaturated fatty acid intake correlated positively with fasting insulin, almost as strongly as saturated fatty acids. Saturated fatty acid intake was highly correlated with monounsaturated fatty acid ($r=0.84$, $p<0.0001$), dietary cholesterol ($r=0.68$, $p<0.0001$), and carbohydrate consumption ($r=-0.68$, $p<0.0001$).

TABLE 2. Measures of Obesity, Insulin, Glucose, Smoking, and Fitness in 215 Nondiabetic Men With Coronary Artery Disease Aged 32–74 Years

Variable	Mean±SD	Range
Body mass index (kg/m^2)	26.7±3.4	20.4–41.1
ΔBody mass index since age 20 years (kg/m^2)	3.6±3.6	−11.0–20.0
Waist-to-hip ratio	0.94±0.05	0.85–1.09
Fasting insulin* (pmol/l)	108±65	14–445
Post–glucose load insulin (pmol/l)	872±555	100–3,351
Fasting glucose† (mmol/l)	5.4±0.88	1.8–7.6
Cigarettes smoked per day‡	24.7±17.7	1–60
Pack-years of smoking	41±32	1–135
Post–glucose load glucose (mmol/l)	8.3±2.8	2.8–15.7
Heart rate achieved on treadmill test (beats per minute)	135±24	71–189
METS achieved on treadmill test	9.1±3.2	2.0–18.0

*To convert from pmol/l to μU/mL, divide by 7.175.
†To convert from mmol/l to mg/dl, divide by 0.05551.
‡Cigarettes smoked per day refers to current smokers only. Pack-years of smoking refers to current and ex-smokers only.
METS, multiples of resting energy expenditure.

Age-adjusted Pearson correlation coefficients of smoking and exercise variables and measures of obesity, insulin, and glucose are provided in Table 4. Smoking variables correlated positively with WHR but not with BMI or insulin levels. Self-reported exercise variables did not correlate significantly with insulin. Regular exercise over the previous year was inversely correlated with BMI. Maximum heart rate and MET (multiples of resting energy expenditure) level achieved on treadmill testing correlated significantly and inversely with BMI and fasting insulin.

Age was inversely correlated with BMI ($r=-0.17$, $p=0.01$) but not correlated significantly with ΔBMI ($r=-0.08$), WHR ($r=0.02$), or fasting insulin ($r=-0.07$). BMI and WHR were positively correlated with each other ($r=0.44$, $p<0.0001$).

Multivariate Analysis

Multivariate analysis was used to assess the independent effects of those dietary variables that were most significantly related to fasting insulin using age-adjusted correlations. The highest correlations were for saturated fatty acid intake, monounsaturated fatty acid intake, and dietary cholesterol. Using these as independent variables along with BMI, age, and total daily caloric intake, various models were constructed to predict fasting insulin concentration. Our criterion for determining the best multivariate model was to maximize the percent of the variance in fasting insulin explained while retaining the greatest number of significant independent variables. BMI was used instead of WHR because when they were included simultaneously in a model to predict fasting insulin, BMI was significant (regression coefficient±SEE, 2.73±1.29) but WHR was not.

Neither age nor total daily caloric intake made significant contributions to the model when BMI was already included. When added separately to a model containing BMI, saturated fatty acids (regression coefficient±SEE, 3.3±1.1), monounsaturated fatty acids (regression coefficient±SEE, 3.3±1.0), and dietary cholesterol (regression coefficient±SEE, 0.14±0.06) each significantly increased the percent of the variance explained in fasting insulin. When saturated fatty acids, monounsaturated fatty acids, and dietary cholesterol were added simultaneously to a model including BMI, none of the dietary variables was significant, presumably because of their multicollinearity; however, their combined effects increased the percent of the variance explained from 14% to 19%. The best models contained saturated fatty acids

TABLE 3. Diet Correlated With Measures of Obesity, Insulin, and Glucose in 215 Nondiabetic Men With Coronary Artery Disease Aged 32–74 Years

	Body mass index	ΔBody mass index	Waist-to-hip ratio	Fasting insulin	Insulin 1 hour post	Fasting glucose	Glucose 1 hour post
Total fat (% total calories)	0.12	0.19†	0.18*	0.23‡	0.16*	0.02	0.11
Saturated fatty acids (% total calories)	0.18†	0.23‡	0.21*	0.26‡	0.17*	0.01	0.09
Monounsaturated fatty acids (% total calories)	0.10	0.18†	0.13	0.24‡	−0.03	0.07	0.13
Polyunsaturated fatty acids (% total calories)	−0.04	−0.01	0.04	−0.02	0.24‡	−0.06	0.03
Cholesterol (mg/1,000 calories)	0.16*	0.18†	0.22*	0.23‡	0.19†	0.04	0.06
Carbohydrate (% total calories)	−0.21†	−0.21†	−0.21*	−0.16*	−0.15*	−0.06	−0.11
Protein (% total calories)	0.19†	0.10	0.06	0.12	0.10	0	−0.01
Alcohol (% total calories)	0.03	0	0.03	−0.13	−0.05	0.06	−0.03
Dietary calories/day	−0.15*	0.01	−0.04	−0.12	−0.13	0	−0.03
Adjusted dietary calories/day	NA	0.04	−0.07	−0.11	−0.12	0	−0.02
Fasting insulin	0.36‡	0.31‡	0.22*	...	0.39‡	0.23‡	0.11

*$p<0.05$, †$p<0.01$, ‡$p<0.001$. Pearson correlation coefficients, adjusted for age.

ΔBody mass index, change in body mass index since age 20 years; Insulin 1 hour post, insulin concentration 1 hour after a 100-g oral glucose load; Glucose 1 hour post, glucose concentration 1 hour after 100-g oral glucose load; Adjusted dietary calories/day, partial correlation coefficients for dietary calories per day with the listed variables after adjusting for body weight in kilograms and age; NA, no value is reported here because weight in kilograms is highly correlated with body mass index ($r=0.82$), and this would confound the result of the partial correlation of calories and body mass index. Waist-to-hip ratio correlations have only 128 observations because of incomplete measurement of that variable for the sample.

1 Calorie=4.2 J.

and BMI or monounsaturated fatty acids and BMI (Table 5). These models, which were virtually identical, show that saturated and monounsaturated fatty acid intakes were positively and significantly related to fasting insulin level after adjusting for BMI, accounting for 18% of the variance in fasting insulin. These models were only slightly stronger than the model containing dietary cholesterol and BMI, which accounted for 17% of the variance in fasting insulin.

We explored the independent effects of smoking, alcohol consumption, self-reported exercise, and treadmill test variables on the relation of saturated fatty acid intake and BMI to fasting insulin. When added to a model containing saturated fatty acids and

TABLE 4. Smoking and Exercise Correlated With Measures of Obesity, Insulin, and Glucose in 215 Nondiabetic Men With Coronary Artery Disease Aged 32–74 Years

	Body mass index	ΔBody mass index	Waist-to-hip ratio	Fasting insulin	Insulin 1 hour post	Fasting glucose	Glucose 1 hour post
Cigarettes smoked/day (current level)	0.08	0	0.20*	−0.09	−0.02	−0.01	0.14*
Pack-years of cigarette smoking	0.08	0.03	0.22*	0	0.08	0.11	0.17*
Total exercise (calories/kg/day)	−0.08	−0.06	−0.01	−0.04	−0.03	−0.02	−0.06
Moderate exercise (calories/kg/day)	−0.02	−0.01	0.06	−0.12	0	−0.03	0.06
Hard exercise (calories/kg/day)	−0.06	−0.08	−0.05	−0.03	−0.06	0.02	−0.09
Very hard exercise (calories/kg/day)	0	0.02	−0.02	0.04	0.05	0.08	−0.06
Hard+very hard exercise (calories/kg/day)	−0.04	−0.04	−0.05	0.01	0	0.07	−0.10
Program of regular exercise	−0.19†	−0.14*	−0.08	−0.03	−0.13	−0.04	−0.10
Routinely active life-style	−0.06	0.02	−0.14	−0.03	−0.01	−0.08	−0.01
Heart rate achieved on treadmill test	−0.18†	−0.19†	−0.09	−0.18†	−0.15*	−0.11	−0.08
METS achieved on treadmill test	−0.20†	−0.17*	−0.10	−0.18†	−0.16*	−0.08	−0.12
Duration of exercise on treadmill test	−0.17*	−0.18*	−0.21*	−0.08	−0.09	−0.03	−0.12

*$p<0.05$, †$p<0.01$. Pearson correlation coefficients, adjusted for age.

ΔBody mass index, change in body mass index since age 20 years; Insulin 1 hour post, insulin concentration 1 hour after 100-g oral glucose load; Glucose 1 hour post, glucose concentration 1 hour after 100-g oral glucose load. Waist-to-hip ratio correlations have only 128 observations because of incomplete measurement of that variable for the sample. For explanation of self-reported exercise variables, refer to "Methods" in text. Cigarettes smoked/day and pack-years of smoking applies to entire sample (e.g., a subject who never smoked has a zero value for both variables). METS, multiples of resting energy expenditure.

1 Calorie=4.2 J.

TABLE 5. Multiple Regression Analyses for Fasting Insulin (pmol/l)

Independent variable	β coefficient	Standard error	p
Intercept	−97.38		
Body mass index (kg/m^2)	6.45	1.20	0.0001
Saturated fatty acids (% total calories)	3.30	1.06	0.002
R^2=0.18			
Intercept	−111.21		
Body mass index (kg/m^2)	6.74	1.15	0.0001
Monounsaturated fatty acids (% total calories)	3.30	1.00	0.001
R^2=0.18			

1 Calorie=4.2 J.

BMI, cigarettes smoked per day increased the percent of the variance explained in fasting insulin from 18% to 20% (regression coefficient±SEE, −0.93±0.39) but did not alter the significant independent associations of saturated fatty acids and BMI with fasting insulin. Neither pack-years of smoking, alcohol consumption, nor any of the exercise variables made significant contributions to models containing saturated fatty acid intake and BMI, and they did not affect the associations of saturated fatty acids and BMI with fasting insulin.

Multivariate analyses were performed to test for dietary predictors of BMI in our sample. Spearman correlation coefficients guided the selection of independent variables. Age, total daily caloric intake, and intake of saturated fatty acids, cholesterol, and carbohydrate were chosen. When added separately to models that included age (regression coefficient±SEE, −0.06±0.03) and caloric intake (regression coefficient±SEE, −0.001±0.0004), saturated fatty acids (regression coefficient±SEE, 0.19±0.06), dietary cholesterol (regression coefficient ±SEE, 0.008±0.003), and carbohydrate (regression coefficient±SEE, −0.08±0.02) each significantly increased the percent of the variance explained in BMI. When saturated fatty acids, dietary cholesterol, and carbohydrate were added simultaneously to a model including age and caloric intake, only carbohydrate remained significant. The best model for predicting BMI included age, caloric intake, and carbohydrate. Interestingly, all three variables were negatively related to BMI. The dietary variables related significantly to WHR were saturated fatty acids, dietary cholesterol, and carbohydrate. When all three variables were added to a model to predict WHR or when any two of the three variables were combined, none of the variables was significant. This result was attributed to multicolinearity.

Discussion

One of our central findings is that saturated fatty acid consumption is positively related to insulin concentration independently of obesity in nondiabetic men with coronary artery disease. It is interesting to speculate on the mechanisms by which dietary saturated fatty acids might reduce insulin sensitivity. Isolated adipocytes from rats fed a high saturated fatty acid diet have fewer insulin receptors, decreased glucose transport, and a generalized decrease in the intracellular capacity to oxidize and metabolize glucose compared with cells from rats fed a control diet.[34,35] Fat cells from rats fed a high saturated fatty acid diet bind less insulin compared with cells from rats fed a high glucose diet[36] or high polyunsaturated fatty acid diet.[37] Insulin-stimulated glucose uptake is lower in adipocytes from rats fed a high saturated fatty acid diet versus a high polyunsaturated fatty acid diet.[37] In healthy men, glucose-stimulated insulin secretion is increased after ingestion of saturated fatty acids, and this may be due to a rise in plasma gastric inhibitory polypeptide.[38] Healthy volunteers exhibit decreased binding to monocyte insulin receptors when fed a high calorie diet rich in saturated fatty acids.[19] Feeding a diet with a high ratio of polyunsaturated to saturated fatty acids to diabetics is associated with higher insulin binding compared with that on a low ratio diet.[39] In vitro enrichment of cells with monounsaturated and polyunsaturated fatty acids increases cell membrane fluidity and is associated with an increase in the number of insulin receptors, albeit with some decrease in receptor affinity.[40] Changes in the phospholipid milieu of the cell membrane in which the insulin receptor is embedded may cause alterations in receptor structure,[40] which could affect receptor function. The intake of saturated fatty acids also may enhance the synthesis of estrogens by colonic flora, and this could result in reduced insulin sensitivity.[41]

It is possible that the association between saturated fatty acid consumption and insulin resistance is mediated by another dietary component for which saturated fatty acids are only a marker. Diets that are higher in saturated fatty acids tend to be lower in complex carbohydrate and fiber.[42] The correlation between saturated fatty acids and total carbohydrate in our population was $r=-0.68$. A diet low in fiber may reduce glucose tolerance in diabetics.[43] We did not assess dietary fiber consumption in our subjects. Monounsaturated fatty acid and dietary cholesterol intake were also highly correlated with saturated fatty acid intake in our sample ($r=0.84$, $r=0.68$, respectively), and both were independent predictors of fasting insulin concentration in multivariate analysis when included as the only dietary variable in the

model. Given the above evidence linking saturated (not monounsaturated) fatty acids to insulin resistance, we suspect that monounsaturated fatty acids and dietary cholesterol are markers of saturated fatty acid intake in our subjects and that this explains their relation to fasting insulin concentration. Most foods that are rich in saturated fatty acids are also rich in monounsaturated fatty acids and cholesterol. We are not aware of a plausible biological mechanism to directly link either monounsaturated fatty acid or cholesterol consumption with insulin resistance, but further research on this topic is warranted.

The observation that saturated fatty acid is positively related and carbohydrate intake is negatively related to BMI after adjustment for total energy intake is consistent with other cross-sectional studies.[25,26] One attractive explanation for this observation is that dietary fat is converted more efficiently into body fat than is dietary carbohydrate.[44–48] Dietary fat can be stored in adipose tissue at a metabolic cost of 3% of ingested calories, whereas the metabolic cost of storing dietary carbohydrate as fat requires the expenditure of 23% of ingested carbohydrate calories.[44] Another possible mechanism is that there is a lower resting metabolic rate and thermic effect of food from a diet rich in fat versus a diet rich in carbohydrate.[46] Another conceivable mechanism is that saturated fatty acids influence the level or activity of hormones that affect adipose stores such as lipoprotein lipase,[49] sex hormones,[50] or insulin, as suggested by our data. Again, we speculate that the relation between dietary cholesterol and measures of obesity is explained by its high correlation with dietary saturated fatty acids rather than a true biological effect. Energy intake was negatively correlated with BMI. Other investigators have found a negative correlation between caloric intake and body fatness.[51] These investigators suggested that energy intake is a marker of regular physical activity because they also found a positive correlation between caloric intake and physical work capacity.[51] In our sample, caloric intake was not associated significantly with WHR or with any measure of self-reported exercise (data not shown).

As expected, measures of obesity in our study were positively associated with fasting insulin levels. BMI was a somewhat stronger predictor of fasting insulin than WHR. Given that intake of saturated fatty acids is associated with obesity, it is possible that saturated fatty acids could affect fasting insulin directly and indirectly by contributing to obesity.

Study Limitations

Several limitations to this study should be noted. Our dietary data are self-reported, and this is a source of potential bias. For example, overweight individuals may underreport the amount of fatty food that they eat. If this bias is present, it is possible that the strength of the relation between saturated fatty acids and fasting insulin may be stronger than what we observed. Our physical activity data are also self-reported and subject to reporting bias; this may help explain why we failed to see any significant inverse association between self-reported exercise and insulin concentration as might have been expected. The men in our study had undergone coronary angiography for clinical indications just before being randomized in the trial. It is possible that the dietary information they reported, assuming it was entirely accurate, may reflect recent changes in eating patterns that do not represent lifelong habits. In fact, the dietary intake data indeed suggest that some of the men had made large changes in their diets, whereas others had not. Unfortunately, we do not have information regarding the dietary habits of our subjects before the study. The design of this study is cross-sectional, and this precludes our ability to make conclusions about cause-and-effect relations. Because our sample was a highly selected population of men with coronary artery disease, our findings may not generalize to a healthy population of men and women.

Summary

Our data show that saturated fatty acid intake is associated with elevated fasting insulin levels in nondiabetic men with coronary artery disease and suggest that saturated fatty acids, independently of their effect on obesity, may contribute to the development of insulin resistance and its clinical consequences.

Appendix

Stanford Coronary Risk Intervention Project Investigators and Staff

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