Fasting Serum Insulin in Relation to Components of the Metabolic Syndrome in European Healthy Men: The European Fat Distribution Study

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To investigate the "metabolic" syndrome in different European populations, samples of 38-year-old healthy men were randomly selected from six centers: Gothenburg (Sweden), Warsaw (Poland), Deinze (Belgium), Verona (Italy), Lumiar (Portugal), and Ede (The Netherlands). In total, 515 men were studied. Anthropometric measurements and blood pressure levels were taken by one or two operators in each center after a common operator's training course. Each blood parameter was analyzed in one laboratory. There were significant intercenter differences in mean values for anthropometric parameters, blood pressure, serum lipids (except for low-density lipoprotein [LDL] cholesterol), and fasting insulin. In particular, fasting serum insulin showed the highest values in Sweden and The Netherlands and the lowest values in Italy and Portugal. In pooled men, fasting insulin was strongly related ($P < .001$) to body mass index (BMI), waist to hip (WHR) and waist to thigh (WTR) circumference ratios, serum lipids (except for LDL cholesterol), and blood pressure. On the contrary, there were relevant differences in the correlation of insulin with serum lipids and blood pressure when the data were evaluated for each center. However, generally both in each center and in all centers together all these correlations disappeared after adjustment for BMI, with the exception of the correlation with serum triglycerides. In pooled men, multiple regression analysis showed an independent association of fasting insulin, BMI, and WHR with serum triglyceride ($P < .001$). On the contrary, total, LDL, and high-density lipoprotein (HDL) cholesterol and blood pressure values showed independent associations with BMI and/or WHR but not with fasting insulin in multivariate models. Thus, in conclusion, the metabolic syndrome is widely present in 38-year-old predominantly non-obese European men, but the most aggregating factor seems more likely to be obesity than hyperinsulinemia. In fact, obesity and abdominal fat distribution, rather than hyperinsulinemia, appear to be associated with an unfavorable risk profile (increased total cholesterol, decreased HDL cholesterol, and high blood pressure levels) for cardiovascular disease in these European men.

THE "METABOLIC" SYNDROME is conventionally defined as a combination of hypertension and abnormalities of lipid and glucose metabolism, which are major risk factors for cardiovascular disease.[1,2] This cluster of risk factors is frequently combined with abdominal obesity,[3,4] and is closely associated with insulin resistance and compensatory hyperinsulinemia.[1,2]

All the above factors are very tightly related to each other, and therefore, it is not easy to identify the most aggregating, ie, presumably independent, factor. On the other hand, solving this problem is of crucial importance for understanding pathophysiological mechanisms and undertaking preventive and therapeutic strategies.

We have recently demonstrated that indicators of abdominal fat distribution are associated with unfavorable risk profiles for cardiovascular disease in European men.[5] Furthermore, we have previously shown that there were considerable differences in fatness and body fat distribution in healthy women from different European countries.[6] In those women the metabolic syndrome was widely present, and the fasting insulin concentration was the most clustering factor of this syndrome. In fact, elevated levels of basal insulin were closely associated, independently of adiposity and body fat distribution, with increased triglycerides and total cholesterol and decreased high-density lipoprotein (HDL) cholesterol, but less clearly with blood pressure levels.[7]

In this context, the purpose of this study was to analyze the relationships between fasting insulin concentration and the components of the metabolic syndrome, in 38-year-old healthy European men, and to verify whether those relations were dependent on body mass index (BMI) and/or regional distribution of body fat.

SUBJECTS AND METHODS

Populations

This study included six cities of six European countries: Gothenburg (Sweden), Warsaw (Poland), Deinze (Belgium), Verona (Italy), Lumiar (Portugal), and Ede (The Netherlands). The samples were randomly selected using the voting lists or birth registers of all men born in 1950 and living in the above-mentioned cities. An informative letter was sent to the men, and those who could be reached by telephone were asked to participate in the study. Those who were asked to participate but refused to do so were asked to answer a "nonresponders questionnaire" that included items such as height, weight, socioeconomic status, and chronic illness. In none of the centers were there significant differences between the BMI and educational status of the participants and nonparticipants who answered the telephone questionnaire. All subjects underwent a medical history and physical examination. Acutely ill subjects and patients suffering from chronic illness (including diabetics) or taking drugs known to influence glucose and lipid metabolism or blood pressure were excluded. The number of participants was 83 (response rate, 78%) in Sweden, 94 (94%) in Poland, 94 (81%) in Belgium, 94 (91%) in Italy, 78 (84%) in Portugal, and 72 (74%) in The Netherlands. In

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Submitted July 26, 1993; accepted April 5, 1994.

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0026-0495/95/4401-0008$03.00/0

total, 515 apparently healthy men were studied. More details of the study have been published elsewhere.[5]

Anthropometry

All anthropometric measurements were performed by one or two operators from each participating center after operators' training in The Netherlands. Circumferences were measured in duplicate on subjects in the standing position, at the end of an expiration. Of the seven circumferences that were measured, we concentrate in this report on the waist circumference (midway between the lower rib margin and the iliac crest), hip circumference (widest circumference over the great trochanters), and thigh circumference (around the right thigh at the level of the gluteal fold). The triceps, biceps, subscapular, suprailiac, and mesogastric skinfolds were also measured, but those data did not add anything to the findings obtained with the circumferences. Therefore, for the sake of clarity, skinfold data were not included in this report. More details about the anthropometric measurements have been presented elsewhere.[8]

Blood Sampling and Analysis

Venous blood was sampled between 8:00 and 8:30 AM after an overnight fast. On the day of the blood sampling, the following parameters were tested as pathological markers: packed cell volume, hemoglobin, white blood cell count, glutamic oxaloacetic transaminase, glutamic pyruvic transaminase, creatinine, and glucose. Blood glucose in particular was not included in the statistical analysis, since no attempt was made to standardize the measurement of this parameter among the six centers. Serum lipids were analyzed in Wageningen (The Netherlands) as described previously.[5] Triglycerides, HDL cholesterol, and total cholesterol levels were determined by enzymatic methods.[9-11] The low-density lipoprotein (LDL) cholesterol level was calculated using the formula of Friedewald et al.[12] Serum insulin concentrations of all the European men who participated in the study were determined in one laboratory in Ghent (Belgium). Frozen serum samples were sent in dry ice to Ghent from all the centers and kept at −80°C until they were analyzed. The insulin level was determined by radioimmunoassay. Serum insulin coefficients of variation were 6.5% intraassay and 9% interassay. The lower limit of sensitivity of the insulin assay was 2.1 μU/mL (15 pmol/L). The cross-reactivity of insulin with proinsulin in this assay was 30%.

Blood Pressure and Behavioral Variables

Blood pressure was measured by one operator in each center with a standard mercury manometer after subjects had rested at least 10 minutes. Systolic blood pressure was recorded at the appearance of sounds, and diastolic blood pressure was recorded at the disappearance of sounds (V-phase Korotkoff). Cuff size was usually 12 × 22 cm, but in the rare instances in which it was necessary, we switched to a larger cuff size. The measurements were repeated after 5 minutes. The average of the measurements was used in analysis. Information on physical activity (at work, leisure time, and sports) and smoking habits (in four categories) was derived from questionnaires as reported elsewhere.[13] These last data are not shown as a table, but they were used in multivariate analysis, as stated in the Results.

Statistical Analysis

Differences between centers were assessed by ANOVA. Differences between pairs of centers were evaluated by Tukey's Studentized range test. Pearson's product-moment correlations and partial correlations were computed using univariate and multiple linear regression analysis. Deviation from normality of the distributions of the variables and the linearity of the relationships (analysis of residuals) were checked. Although some of the variables used in analysis were slightly skewed, only the logarithmic transformation of triglyceride levels improved the fit of the regression models. Therefore, we present analysis with untransformed variables, except for serum triglycerides. P values less than .05 were considered significant. Data are expressed as the mean ± SE.

RESULTS

Tables 1 and 2 show the mean ± SE of anthropometric measurements, serum lipids, blood pressure, and fasting insulin in 38-year-old European men selected from different sites.

ANOVA showed that there were significant differences in all variables studied (except LDL cholesterol) among the

Table 1. Mean ± SE for Anthropometric Measurements, Serum Lipids, Fasting Insulin, and Blood Pressure in 38-Year-Old European Men Selected From Six Cities (N = 515)

	S (n = 83)	PL (n = 94)	B (n = 94)	I (n = 94)	P (n = 78)	NL (n = 72)	F
Anthropometry							
BMI (kg/m²)	23.9 ± 0.3	25.8 ± 0.3	25.3 ± 0.4	25.5 ± 0.3	25.4 ± 0.3	24.7 ± 0.4	3.7†
WHR	0.91 ± 0.01	0.93 ± 0.01	0.92 ± 0.01	0.96 ± 0.01	0.89 ± 0.01	0.93 ± 0.01	19.9‡
WTR	1.53 ± 0.01	1.59 ± 0.02	1.59 ± 0.01	1.57 ± 0.01	1.45 ± 0.01	1.59 ± 0.01	19.0‡
Serum lipids (mmol/L)							
Triglycerides	1.10 ± 0.07	1.40 ± 0.08	1.30 ± 0.08	1.40 ± 0.09	1.23 ± 0.08	1.53 ± 0.11	2.8*
Total cholesterol	5.70 ± 0.11	5.73 ± 0.11	5.96 ± 0.11	6.21 ± 0.13	5.80 ± 0.13	5.81 ± 0.14	2.6*
LDL cholesterol	3.87 ± 0.09	3.89 ± 0.11	4.08 ± 0.10	4.24 ± 0.11	3.97 ± 0.11	3.89 ± 0.12	1.6
HDL cholesterol	1.27 ± 0.03	1.18 ± 0.03	1.27 ± 0.03	1.33 ± 0.03	1.21 ± 0.03	1.18 ± 0.03	4.0†
Serum insulin (μU/mL)	20.0 ± 0.61	18.8 ± 0.63	18.6 ± 0.56	16.0 ± 0.65	17.1 ± 0.54	19.0 ± 0.62	5.5‡
Blood pressure (mm Hg)							
Systolic	126.6 ± 1.4	131.7 ± 1.4	123.3 ± 1.3	133.2 ± 1.5	134.1 ± 1.8	133.8 ± 1.5	9.6‡
Diastolic	80.5 ± 0.8	85.6 ± 1.0	79.3 ± 1.0	86.7 ± 0.9	84.8 ± 1.2	80.5 ± 1.2	9.6‡

NOTE. F values of ANOVA for the comparison among centers are reported.

Abbreviations: S, Sweden; PL, Poland; B, Belgium; I, Italy; P, Portugal; NL, The Netherlands.

*$P < .05$.

†$P < .01$.

‡$P < .001$.

Table 2. Mean ± SE and Range for Anthropometric Parameters, Serum Lipids, Fasting Insulin, and Blood Pressure in Pooled European Men (N = 515)

	Mean ± SE	Range
Anthropometry		
BMI (kg/m²)	24.5 ± 0.04	15.3-43.8
WHR	0.92 ± 0.01	0.77-1.11
WTR	1.55 ± 0.01	1.02-1.97
Serum lipids (mmol/L)		
Triglycerides	1.2 ± 0.10	0.23-7.31
Total cholesterol	5.9 ± 0.13	2.78-10.2
LDL cholesterol	4.0 ± 0.10	0.96-7.39
HDL cholesterol	1.2 ± 0.03	0.69-2.34
Serum insulin (μU/mL)	18.2 ± 0.06	2.54-54.1
Blood pressure (mm Hg)		
Systolic	130.2 ± 1.5	95.0-206.0
Diastolic	83.0 ± 1.0	51.0-117.0

centers. In particular, basal insulin showed significant intercenter differences: the lowest value was found in Italian men (16.0 ± 0.65 μU/mL), who had a significantly lower fasting insulin than men from any other center (except Portugal). Furthermore, fasting insulin was significantly lower in men from Portugal than in Swedish and Dutch men, whereas no statistical difference in fasting insulin was found among the men from Sweden, Poland, and The Netherlands. The highest mean fasting insulin concentration was observed in Sweden (20.0 ± 0.61 μU/mL).

Table 3 displays the simple correlation coefficients of fasting insulin levels with anthropometric measurements, serum lipids, and blood pressure. All anthropometric parameters were significantly correlated with serum insulin both in pooled subjects and in each separate center (except for waist to thigh ratio [WTR] in four centers and waist to hip ratio [WHR] in one center). Fasting insulin was also strongly associated with both serum lipids (except LDL cholesterol) and blood pressure, when the data were analyzed for pooled centers. On the contrary, there were relevant differences when the data were evaluated for each center.

Generally, both in each center and in pooled subjects, the associations of fasting insulin with serum lipids and blood pressure disappeared in bivariate analysis after adjustment for BMI, with the exception of the association with serum triglyceride levels. In fact, when the men were pooled, a significant partial (BMI-adjusted) correlation between fasting insulin and serum triglycerides ($r = .15, P < .001$) was observed, whereas no significant partial correlation was found between fasting insulin and total, LDL, and HDL cholesterol or between fasting insulin and blood pressure levels. Of all anthropometric measurements, only the WTR showed a weak partial (BMI-adjusted) correlation with fasting serum insulin ($r = .10, P < .05$).

Tables 4 and 5 show data from a multivariate analysis we performed in pooled men. WHR, BMI, and fasting insulin were included as independent variables to predict serum lipids and blood pressure. In that model, WHR was independently related to all variables, except HDL cholesterol concentration; BMI was independently related to all variables except total and LDL cholesterol level; and fasting insulin was independently related only to serum triglycerides. Similar results were obtained when WTR replaced WHR in the multivariate models (data not shown). Notably, substantially the same results were obtained even when physical activity, cigarette smoking, and "centers" (introducing dummy variables for each center) were taken into account in previous regression models (data not shown). As a matter of fact, the only parameter clearly and consistently associated with fasting insulin after adjustment for all potential confounders was serum triglycerides.

DISCUSSION

This study showed that there were significant differences in fasting insulin concentrations among different European cities: the lowest value was found in Italy and Portugal and the highest in Sweden and The Netherlands. It should be noted that all serum insulin determinations were per-

Table 3. Pearson's *r* Values for the Simple Correlations of Fasting Insulin With Anthropometric Parameters, Serum Lipids, and Blood Pressure in European Men Aged 38 Years

	S (n = 83)	PL (n = 94)	B (n = 94)	I (n = 94)	P (n = 78)	NL (n = 72)	All (n = 515)
Anthropometry							
BMI	.53‡	.45‡	.38‡	.39‡	.30†	.52‡	.37‡
WHR	.36†	.32*	.29*	.11	.33†	.45‡	.21‡
WTR	.29*	.19	.17	.06	.35†	.44‡	.21‡
Serum lipids							
Log triglycerides	.32†	.32†	.43‡	.06	.37†	.41‡	.29‡
Total cholesterol	.41†	.25*	.06	−.01	.22	.19	.12†
LDL cholesterol	.29†	.12	−.06	.01	.24*	.06	.05
HDL cholesterol	−.03	−.03	−.16	−.20*	−.27*	−.26*	−.16‡
Blood pressure							
Systolic	.23*	.34†	.34‡	.14	.20	.03	.16‡
Diastolic	.25*	.35‡	.28†	.14	.27	.11	.17‡

Abbreviations: S, Sweden; PL, Poland; B, Belgium; I, Italy; P, Portugal; NL, The Netherlands.
*$P < .05$.
†$P < .01$.
‡$P < .001$.

Table 4. Multiple Regression Analysis in Pooled Men: Linear Regression Coefficients ± Standard Error (β ± SE) Adjusted for WHR, BMI, and Fasting Insulin in Relation to Blood Lipids in European Men (N = 515)

Dependent Variable	Independent Variable	Regression Coefficient β	SE	t
Log triglycerides	WHR	2.01	0.51	3.91‡
	BMI	0.04	0.009	4.79‡
	Insulin	0.015	0.004	3.36‡
	Intercept	−3.07	0.40	
Total cholesterol	WHR	4.58	1.07	4.29‡
	BMI	0.024	0.019	1.27
	Insulin	0.010	0.009	1.03
	Intercept	0.85	0.84	
HDL cholesterol	WHR	0.10	0.27	0.36
	BMI	−0.022	0.005	−4.58‡
	Insulin	−0.003	0.002	−1.57
	Intercept	1.76	0.21	
LDL cholesterol	WHR	3.05	0.97	3.15†
	BMI	0.020	0.017	1.18
	Insulin	−0.001	0.008	−0.04
	Intercept	0.67	0.77	

*$P < .05$.
†$P < .01$.
‡$P < .001$.

formed in one laboratory, and that we previously checked the storage length and conditions of serum samples.[7] Also, in a previous study on 38-year-old European women, participants from Verona showed the lowest mean fasting insulin, whereas the highest value was found in women from The Netherlands and Poland.[7] We have no clear explanation for finding the lowest value of fasting insulin in both Italian men and women. This was certainly not due to differences in BMI or body fat distribution, since both Italian men and women had the highest mean values for BMI and WHR; therefore, the possible adjustment for BMI and WHR, which were both positively related to the basal insulin concentration, would only be able to magnify the observed differences in insulin levels between Italian and other European men. Recently, Facchini et al[14] have demonstrated that chronic cigarette smokers were insulin-resistant, hyperinsulinemic, and dyslipidemic compared with a matched group of nonsmokers. This was not observed in our multicenter study, since the Italian men were among those with the heaviest smoking habit[13] and at the same time had the lowest fasting insulin. Furthermore, dietary factors, for example, the carbohydrate to lipid ratio of the diet, were also demonstrated to influence insulin sensitivity and serum insulin concentrations, thus consequently contributing to the development of type II diabetes mellitus.[15-17] Unfortunately, in our study no attempt was made to obtain reliable information about the dietary intake, and therefore, we were unable to appreciate the possible influence of eating behavior on serum insulin. Genetic susceptibility could obviously be involved as well.[18] In fact, it was shown that Mexican-Americans had higher mean levels of serum insulin[19] and a more centralized and upper-body adiposity[20] as compared with non-Hispanic whites. Here an opposite trend has been shown, with serum insulin being lower in southern than in northern Europe.

Table 5. Multiple Regression Analysis in Pooled Men: Linear Regression Coefficients ± Standard Error (β ± SE) Adjusted for WHR, BMI, and Fasting Insulin in Relation to Blood Pressure in European Men (N = 515)

Dependent Variable	Independent Variable	Regression Coefficient β	SE	t
Systolic blood pressure	WHR	28.8	13.6	2.11*
	BMI	0.90	0.24	3.73‡
	Insulin	0.16	0.12	1.38
	Intercept	78.1	10.7	
Diastolic blood pressure	WHR	20.0	9.3	2.16*
	BMI	0.78	0.16	4.78‡
	Insulin	0.08	0.08	0.99
	Intercept	43.4	7.2	

*$P < .05$.
†$P < .01$.
‡$P < .001$.

This multicenter study confirmed that the components of the metabolic syndrome were closely interrelated in men from different European countries. As a matter of fact, in pooled subjects, fasting insulin was positively associated with BMI, abdominal fat distribution, serum lipids, and blood pressure. We find it remarkable that these findings were observed in a sample of nondiabetic and predominantly non-obese men; moreover, the random selection of samples and the homogeneous age could enhance the validity of our findings. In this study, basal insulin was used as a marker of insulin sensitivity, and consequently of insulin resistance. Obviously, this could be questionable. However, in nondiabetic subjects fasting insulin was moderately correlated with the degree of insulin sensitivity as measured by the euglycemic clamp technique ($r = .60$).[21] Furthermore, Wing et al[22] showed that fasting insulin was more strongly associated with several cardiovascular risk factors than post–glucose load insulin levels. On the other hand, and also recently, several prospective epidemiological studies have used basal insulin as a marker of insulin resistance.[19,23]

The main aim of the present study was to verify whether the relationship between fasting insulin and the components of the metabolic syndrome was influenced by adiposity and body fat distribution.

We found that no significant associations between baseline insulin and total, LDL, and HDL cholesterol levels were observed after adjustment for overall adiposity. Generally, the lack of a relationship was noted both in pooled men and in subjects from each center (except for HDL cholesterol in Italy and The Netherlands and total cholesterol in Sweden).

The lack of a correlation between fasting insulin and total or LDL cholesterol was consistent with the notion that hypercholesterolemia is not frequently associated with hyperinsulinemia and insulin resistance.[1,2,23,24] Recently, Karhapää et al,[25] by means of euglycemic clamp studies, found that subjects with isolated hypercholesterolemia have the same insulin sensitivity as control subjects without hypercholesterolemia. Perhaps the major relevance in our

study of adiposity rather than hyperinsulinemia on main cardiovascular risk factors was suggested also by the lack of a significant correlation between fasting insulin and HDL cholesterol after adjustment for BMI: this was in contrast to the findings of several studies in other more homogeneous populations or in selected samples of patients.[1,2,23,24] However, other investigators obtained similar results.[26] Interestingly, this finding disagrees also with what we found in European women of the same age.[7] In fact, in those women the relationship between fasting insulin and plasma triglycerides, total cholesterol, and HDL cholesterol was independent of overall adiposity.

In accordance with the majority of the studies, the present report confirmed a positive partial correlation between fasting insulin and serum triglycerides.[1,2,23,24] We do find that serum insulin is an independent predictor of triglyceride levels, confirming the evidence that insulin stimulates hepatic very-low-density lipoprotein secretion.[1,2,27] The lack of such a correlation in Italian men remains unclear. It should be noted that all sera for the determination of both lipids and insulin were tested in one laboratory. Moreover, both insulin and triglyceride serum levels were also analyzed in fresh blood samples in a laboratory in Verona, and also in that case triglycerides and insulin levels were not correlated. A different influence of genetic and environmental factors (dietary intake, alcohol consumption, smoking habits, etc.) on the relations between fasting insulin and serum lipids (especially triglycerides) could partially explain those differences.

The association of increased serum insulin with high blood pressure is a recent finding supported by several studies.[1,2,28,29] On the contrary, the correlations of blood pressure with adiposity and body fat distribution are well-known and old findings.[3] Nevertheless, the link between hyperinsulinemia and hypertension is still incompletely understood. Recently, Jarrett hypothesized that the association between serum insulin and blood pressure in epidemiological studies is probably due to common associations with other variables, of which abdominal obesity and lean body mass are statistically the most important.[30] Haffner et al[31] have not found any BMI-adjusted correlation between fasting insulin and blood pressure in women of the San Antonio Heart Study, whereas the correlation was significant in men. However, in this case, the association between fasting insulin and hypertension was independent of adiposity in lean subjects but not in the overall population after adjustment for adiposity.[23] In the study by Folsom et al[26] on approximately 1,100 black and another 1,100 white predominantly non-obese subjects aged 18 to 30 years, there were low-order univariate correlations between fasting insulin and blood pressure in both groups, but inclusion of serum insulin in multivariate regression models made little difference in the stronger associations between body fat or fat distribution and blood pressure.

Significant associations between fasting insulin and both systolic and diastolic blood pressure levels were observed also in our study, but in bivariate analysis those associations generally disappeared after matching for BMI both in pooled men and in each center. These findings were also in agreement with the data from our previous study in European women.[7] Thus, in both sexes the correlation between fasting insulin and blood pressure is widely diminished after adjustment for adiposity.

At this point, one might be tempted to conclude that obesity per se seems even more strongly related to a cluster of metabolic disorders than hyperinsulinemia. However, abdominal distribution of body fat may increase the risk of obesity's producing metabolic abnormalities. Several epidemiological studies have demonstrated that abdominal fat distribution predisposes subjects toward metabolic disorders such as glucose intolerance, hypertension, and dyslipidemia, which are known risk factors for cardiovascular disease.[3,4,32,33] We have also previously shown that indicators of body fat distribution are associated with an unfavorable risk profile for cardiovascular disease in these European men.[5]

To verify whether body fat distribution could add something to these associations, a multivariate analysis was performed. WHR, BMI, and fasting insulin were included as covariates to predict serum lipids and blood pressure. WHR was independently related to all variables except HDL cholesterol. BMI was independently related to all variables except total and LDL cholesterol, and serum insulin was independently related only to triglycerides.

Since we demonstrated significant intercenter differences for most variables studied, the analysis of pooled men from six centers could be questionable. However, although statistically significant, these differences are not great from a clinical standpoint; furthermore, we have verified that our analyses of data produced substantially similar results when adjusted for "centers." Here it should be noted that if two variables, eg, BMI and insulin in this study, are independently and equally associated with a third one, it could be that the one of the first two variables that is more precisely measured will sort out as the variable more significantly related to the third one. Nevertheless, our results suggest that there are considerable differences in the relationships between fasting insulin and the components of metabolic syndrome in 38-year-old European men and women despite the same variables and methods.[7] In fact, in those women basal insulin was correlated with all the components of the metabolic syndrome, and after adjustment for obesity and body fat distribution, fasting insulin continued to be the most aggregating and independent factor of this syndrome.

We have previously shown that smoking habits and physical activity are significantly related to body fat distribution and may be potential confounders in the relations between fat distribution and other cardiovascular risk factors.[13] Interestingly, in the present study the adjustment for those behavioral variables did not improve the fit of regression models.

In conclusion, this study showed that at least in 38-year-old predominantly non-obese European men, fasting insulin was related to the components of the metabolic syndrome, but most of these associations disappeared after adjustment for BMI and WHR. These results support the possibility that obesity and abdominal fat distribution, rather than hyperinsulinemia, are associated with an unfa-

vorable risk profile (increased total cholesterol, decreased HDL cholesterol, and high blood pressure levels) for cardiovascular disease in European men.

ACKNOWLEDGMENT

The authors thank Professors Joseph G.A.J. Hautvast, Victor Szostak, Ludovico A. Scuro (deceased), and Albert Vermeulen for their contributions to the organization of the study. They also thank the participating municipalities for their cooperation. The participation of the Project Management Group of "Euro Nutrition" (EURO-NUT), a concerted action project on nutrition and health of the Comac-Epidemiology Group within the Medical Research Council of the European Community, is gratefully acknowledged.

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