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Insulin resistance, serum adiponectin, and proinflammatory markers in young subjects with the metabolic syndrome

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Abstract

Insulin resistance is the underlying metabolic abnormality in the metabolic syndrome. The low-grade chronic inflammation may be associated with metabolic risk factors and atherogenesis. The aim of our study was to establish the link between the metabolic syndrome, as defined by the National Cholesterol Education Program (NCEP) criteria, and insulin sensitivity, serum adiponectin, and parameters of chronic inflammation in young subjects. The group of 223 subjects (mean age, 25.86 ± 5.49 years; body mass index, 28.04 ± 6.91 kg/m2) was studied. Oral glucose tolerance test, euglycemic hyperinsulinemic clamp, and estimation of serum adiponectin and proinflammatory factors were performed. The NCEP-defined metabolic syndrome was present in 49 subjects (21.97%). The higher the number of NCEP criteria fulfilled was, the bigger were the decrease in insulin sensitivity ($P < .0001$) and adiponectin ($P < .0001$) and the increase in fasting and postload insulin (both Ps < .0001), C-reactive protein ($P < .0001$), interleukin 18 ($P < .0001$), interleukin 6 ($P < .0001$), and soluble tumor necrosis factor–α receptors sTNFR1 ($P < .0001$) and sTNFR2 ($P < .0001$) observed. Multiple regression analysis revealed that adiponectin and inflammatory factors predicted NCEP score independent of insulin sensitivity (all adjusted β values between .16 and .32, all Ps < .01). Young subjects with metabolic syndrome demonstrate an increased inflammatory response and lower adiponectin concentration.

1. Introduction

The *metabolic syndrome* (MS) is defined as a coexistence of criteria/symptoms, which taken together or analyzed separately increase the risk of cardiovascular disease. In the United States, the overall prevalence of MS in adults exceeds 20% and increases with age and body mass index (BMI) [1]. The first description of coincidence of risk factors (elevated blood pressure, dyslipidemia, and impaired glucose tolerance [IGT]), which increases the risk of cardiovascular complications, was given by Reaven [2]. Over the recent years, different groups have proposed inclusion of numerous criteria into the diagnosis of MS [3-6]. Commonly used in clinical practice are the criteria proposed by the National Cholesterol Education Program (NCEP) Adult Treatment Panel (ATP) III [5]. The accumulated evidence indicates that insulin resistance is an important pathogenic factor for MS, although a precise mechanism linking particular component of MS with insulin resistance is not fully understood [2]. Low-grade chronic inflammation is considered to be a common background in both insulin resistance and atherogenesis [7]. It is suggested that systemic inflammation mediates numerous pathogenic mechanisms responsible for the association between MS components. There are observations that the sensitive marker of systemic inflammation C-reactive protein (CRP) is elevated in patients with obesity and MS [8]. C-reactive protein is also considered to be an independent predictor for coronary heart disease and type 2 diabetes mellitus [9,10]. One of the concepts is that there is a chronic inflammation, which induces insulin resistance in obesity [7,11]. Another hypothesis is that the inflammatory process could be induced by up-regulation of metabolic alterations (glucose, lipids, blood pressure) emanating from insulin resistance. Expanded adipose tissue can be a source of proinflammatory cytokines, which could play a role in the development of insulin resistance as well as atherogenesis [11]. There are studies showing an increased

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adipose tissue expression of tumor necrosis factor–α (TNF-α) in human obesity as well as an increased plasma concentration of its soluble receptors sTNFR1 and sTNFR2 [12]. Similar observations were made for other proinflammatory markers—interleukin 6 (IL-6) [13] and interleukin 18 (IL-18) [14]. Adipose tissue is also a source of adiponectin, which has anti-inflammatory and cardioprotective properties and might play a protective role in the development of insulin resistance and type 2 diabetes mellitus [15]. A diminished level of adiponectin was noticed in human obesity, type 2 diabetes mellitus, and coronary heart disease [16,17].

An elevated concentration of CRP and other proinflammatory markers, together with hypoadiponectinemia, is already present in very young obese children and adolescents, suggesting that the development of insulin resistance could start at an early age [18,19]. Taking into account the epidemic of human obesity, an early identification of the patients with high risk of cardiovascular complications is necessary. Therefore, we aimed to establish the relationships between the MS, as defined by the NCEP criteria, and insulin sensitivity, serum adiponectin, and parameters of chronic inflammation in young subjects.

2. Subjects and methods

2.1. Study group

We examined 223 subjects (147 women and 76 men) between 18 and 40 years of age. The participants were recruited from the outpatient clinic of the Department of Endocrinology, Diabetology, and Internal Medicine, Medical University of Bialystok, Poland, from the collaborating primary care practice and from the medical staff and students. None of the participants had cardiovascular disease, unstable hypertension, previously apparent disturbances of glucose metabolism, infections, or any other serious medical problems. All subjects were nonsmokers and were not taking any anti-inflammatory drugs within the previous 3 months. Before entering the study, physical examination and appropriate laboratory tests were performed. Analyses were performed after an overnight fast. Glucose tolerance was assessed on the basis of fasting plasma glucose and oral glucose tolerance test according to the American Diabetes Association criteria. In the study group, 184 subjects had normal glucose tolerance, 19 had impaired fasting glucose (IFG), 12 had IGT (of whom 6 also had IFG), and 8 was diagnosed with type 2 diabetes mellitus. The study protocol was approved by the Ethics Committee of the Medical University of Bialystok, Poland. All subjects gave an informed written consent before entering the study. We certify that all applicable institutional and governmental regulations concerning the ethical use of human volunteers were followed during this research.

2.2. Anthropometry

Body mass index was calculated as body weight × height^{-2} and expressed in kilograms per square meter. The waist circumference was measured at the smallest circumference between the rib cage and iliac crest, with the subject in the standing position. The percentage of body fat was calculated by bioelectric impedance analysis using the Tanita TBF-511 Body Fat Analyzer (Tanita, Tokyo, Japan).

2.3. Insulin sensitivity

Insulin sensitivity was measured by the euglycemic hyperinsulinemic clamp technique according to DeFronzo et al [20], as described previously [21]. On the morning of the study, 2 venous catheters were inserted into antecubital veins, one for the infusion of insulin and glucose and the other in the contralateral arm for blood sampling; the arm was heated to approximately 60°C. Insulin (Actrapid HM; Novo Nordisk, Copenhagen, Denmark) was given as a primed-continuous intravenous infusion for 2 hours at 40 mU/(m^2 min), resulting in constant hyperinsulinemia of approximately 75 μIU/mL. Arterialized blood glucose was obtained every 5 minutes, and 20% dextrose (1.11 mol/L) infusion was adjusted to maintain plasma glucose levels at 90 mg/dL. The glucose infusion rate approached stable values during the final 40 minutes of the study, and the rate of whole-body glucose uptake (*M* value) was calculated as the mean glucose infusion rate from 80 to 120 minutes corrected for glucose space and normalized per kilogram of fat-free mass (ffm).

2.4. Biochemical analyses

Fasting blood samples were taken from the antecubital vein before the beginning of the clamp to determine serum lipids, IL-18, IL-6, soluble forms of TNF-α receptors (sTNFR1 and sTNFR2), adiponectin, and CRP. The samples were kept frozen at −70°C until analyses.

Plasma glucose was measured immediately by the enzymatic method using glucose analyzer (YSI 2300 STAT Plus, Yellow Springs, OH). Serum insulin was measured with the monoclonal immunoradiometric assay (Medgenix Diagnostics, Fleunes, Belgium). Serum total and high-density lipoprotein (HDL) cholesterol and triglycerides (TG) were assessed by enzymatic methods (Cormay, Warsaw, Poland). Serum low-density lipoprotein cholesterol was calculated according to the Friedewald formula. Serum free fatty acids (FFA) were measured with the colorimetric method, as reported previously [21].

Serum IL-18 concentration was measured with the enzyme-linked immunosorbent assay (ELISA) kit (Quantikine; R&D Systems, Minneapolis, MN) with a detection limit less than 12.5 pg/mL and with intraassay and interassay coefficients of variation (CVs) less than 11%. Serum IL-6 was estimated with the high-sensitive ELISA (Quantikine HS, R&D Systems) with a detection limit of 0.039 pg/mL and with intraassay and interassay CVs less than 6.9% and

Table 1
Clinical, metabolic, and inflammatory parameters in the groups with and without MS

Parameter	MS (+) n = 49	MS (−) n = 174
Age (y)	29.94 ± 6.70*	24.71 ± 4.50
BMI (kg/m^2)	36.46 ± 5.86*	25.67 ± 5.10
Waist girth (cm)	109.18 ± 13.49*	83.37 ± 12.27
SBP (mm Hg)	136.39 ± 20.69*	121.98 ± 10.08
DBP (mm Hg)	89.83 ± 13.02*	79.22 ± 6.66
sTNFR1 (ng/mL)	2.30 ± 0.66*	1.90 ± 0.37
sTNFR2 (ng/mL)	7.31 ± 2.69*	5.63 ± 1.85
hs-CRP (ng/mL)	4.82 ± 3.71*	2.16 ± 2.68
IL-18 (ng/mL)	319.43 ± 132.72*	257.12 ± 122.53
hsIL-6 (pg/mL)	2.57 ± 2.03*	1.58 ± 1.71
Adiponectin (μg/mL)	10.38 ± 4.63*	16.40 ± 8.74
M_{ffm} (mg/[kg min])	4.88 ± 2.68*	9.37 ± 3.65
Glucose 0 (mg/dL)	104.46 ± 22.29*	85.64 ± 9.89
Glucose 120 (mg/dL)	134.40 ± 55.18*	85.92 ± 21.33
Insulin 0 (mU/L)	20.94 ± 11.33*	11.19 ± 7.54
Insulin 120 (mU/L)	111.78 ± 93.15*	38.40 ± 34.35
FFA 0 (mmol/L)	597.75 ± 195.22	543.48 ± 207.13
FFA 120 clamp (mmol/L)	270.94 ± 142.94*	192.09 ± 117.76
Total cholesterol (mg/dL)	196.20 ± 38.98	184.71 ± 35.93
TG (mg/dL)	189.97 ± 150.37*	88.42 ± 50.67
HDL cholesterol (mg/dL)	39.32 ± 6.95*	56.02 ± 12.07
LDL cholesterol (mg/dL)	120.29 ± 34.71	109.48 ± 32.91

Data are presented as mean ± SD. SBP indicates systolic blood pressure; DBP, diastolic blood pressure.

* $P < .05$ for the differences between subjects with and without MS.

9.6%, respectively. Serum sTNFR1 and sTNFR2 were determined with the enzyme amplified sensitivity immunosorbent assay kits (BioSource Europe, Nivelles, Belgium). Serum adiponectin was measured with radio immunoassay kit (Linco Research, St Charles, MO) with a detection limit of 1 ng/mL and with intraassay and interassay CVs less than 6.3% and 9.5%, respectively. Serum CRP was estimated with the high-sensitive ELISA kit (high-sensitivity CRP [hs-CRP]; Euroimmun, Luebeck, Germany) with a detection limit of 0.8 ng/mL and with intraassay and interassay CVs less than 7.8%.

2.5. Diagnosis of MS

The diagnosis of MS was based on the NCEP criteria [5]. Metabolic syndrome was diagnosed when 3 of the following 5 criteria were fulfilled:

1. Waist circumference greater than 102 cm in men and greater than 88 cm in women
2. Blood pressure at least 130/85 mm Hg
3. Serum TG at least 150 mg/dL
4. High-density lipoprotein cholesterol less than 40 mg/dL in men and less than 50 mg/dL in women
5. Fasting plasma glucose at least 100 mg/dL.

The last criterion, fasting plasma glucose, was changed to 100 mg/dL from the initial cutoff point of 110 mg/dl, according to the revised guidelines [22].

2.6. Statistical analysis

The statistic analyses were performed with the STATISTICA 7.0 (Statsoft, Krakow, Poland) program. The variables that did not have normal distribution (M value, IL-18, IL-6, hs-CRP, fasting and postload insulin, and TG) were log-transformed before analyses. For the purpose of data presentation, these variables were again transformed to absolute values in the section "Results." The differences between groups with and without NCEP-defined MS were evaluated with the unpaired Student t test. Differences in relation to NCEP score (from 0 to 5) were estimated with 1-way analysis of variance. The relationships between variables were assessed with the Pearson product-moment correlation analysis and with multiple regression analysis. The level of significance was accepted at P value less than .05.

3. Results

From the study population (N = 223), 49 (21.9%) subjects (35 women and 14 men) met the NCEP ATP III criteria for MS. The prevalence of MS according to the glucose tolerance status was as follows: 21 subjects of 184 in the group with normal glucose tolerance, 10 of 19 in the IFG group, 10 of 12 in the IGT group (including all 6 subjects who also had IFG), and all 8 subjects with type 2 diabetes mellitus. The prevalence of the individual MS criteria in the group with the MS as defined by NCEP ATP III was as follows: most frequently, the subjects complied with the criterion of waist girth (91.83%), then HDL cholesterol (87.75%), blood pressure (73.5%), TG (57.14%), and glucose (53.06%).

Table 2
Studied parameters in dependence of NCEP score (analysis of variance)

NCEP score	0 (n = 80)	1 (n = 60)	2 (n = 34)	3 (n = 21)	4 (n = 25)	5 (n = 3)	P
Insulin 0 (mU/L)	9.25 ± 4.52	10.46 ± 4.99	16.67 ± 12.54	20.87 ± 14.76	19.67 ± 7.43	31.0 ± 6.39	<.000001
Insulin 120 (mU/L)	30.2 ± 26.8	38.3 ± 33.6	56.3 ± 43.3	100.6 ± 116.1	111.6 ± 59.9	219.7 ± 125.3	<.000001
M_{ffm} (mg/[kg min])	9.87 ± 3.62	9.64 ± 3.77	7.74 ± 3.11	6.12 ± 3.09	4.14 ± 1.91	2.40 ± 0.79	<.000001
hs-CRP (ng/mL)	1.27 ± 1.85	2.31 ± 2.67	3.48 ± 3.39	3.34 ± 3.32	5.56 ± 3.68	8.51 ± 3.52	.000009
IL-18 (ng/mL)	240.5 ± 117.8	235.1 ± 86.0	334.8 ± 156.9	269.5 ± 89.2	350.9 ± 146.9	406.8 ± 184.9	.000017
hsIL-6 (pg/mL)	1.61 ± 2.09	1.56 ± 1.50	1.56 ± 1.01	2.25 ± 1.30	2.87 ± 2.55	2.30 ± 0.46	.00009
Adiponectin (μg/mL)	17.23 ± 8.04	16.22 ± 7.73	14.75 ± 11.58	11.75 ± 5.05	9.04 ± 3.88	10.17 ± 5.76	.00001
sTNFR1 (ng/mL)	1.85 ± 0.36	1.87 ± 0.35	2.04 ± 0.37	2.20 ± 0.53	2.35 ± 0.77	2.60 ± 0.36	.000001
sTNFR2 (ng/mL)	5.45 ± 1.91	5.71 ± 1.62	5.92 ± 2.10	7.24 ± 2.54	7.33 ± 2.89	7.57 ± 3.02	.0002

Data are presented as mean ± SD.

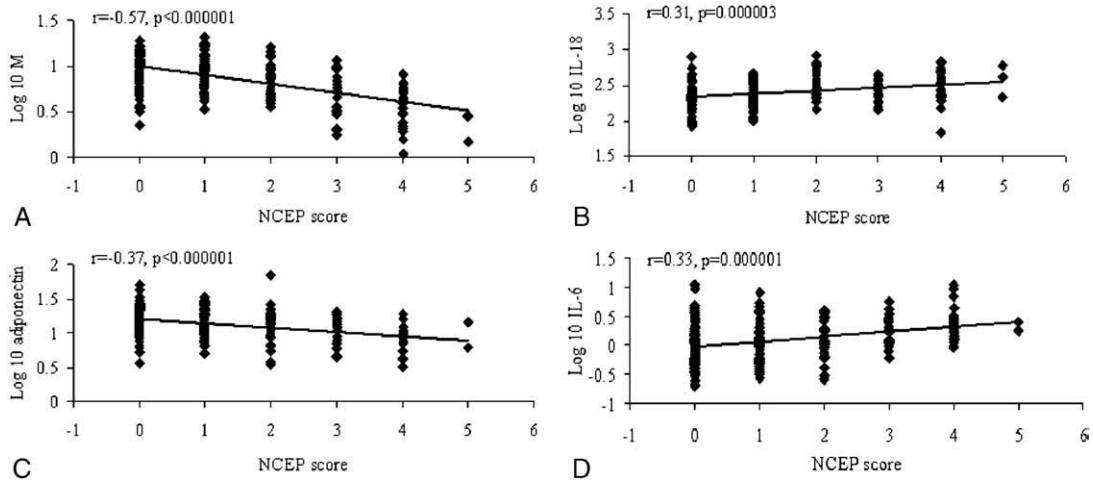

Fig. 1. Relationships between NCEP score and log 10–transformed parameters: *M* value (A), IL-18 (B), adiponectin (C), and IL-6 (D) in the studied population (N = 223).

Insulin sensitivity index (M_{ffm}) was markedly diminished in the group with MS ($P < .0001$). Fasting glucose and insulin, as well as postload concentration, differed markedly according to the presence of MS, being significantly higher in patients with MS ($P < .0001$ for all comparisons) (Table 1). There was no difference in fasting FFA concentration; however, during the clamp studies, the suppression of FFA release was markedly higher in the group without MS ($P = .00086$) (Table 1). Further comparison of the groups for the presence of MS revealed significantly lower adiponectin ($P < .0001$) and higher sTNFR1 ($P < .0001$), sTNFR2 ($P < .0001$), hs-CRP ($P < .0001$), IL-18 ($P = .0017$), and IL-6 ($P < .0001$) levels in subjects with MS (Table 1).

Analysis of variance revealed that, together with the increase in the number of NCEP criteria, there was a significant decrease in insulin sensitivity ($P < .0001$) and adiponectin ($P < .0001$) and an increase in fasting and postload insulin concentrations (both *P*s < .0001), sTNFR1 ($P < .0001$), sTNFR2 ($P = .0002$), hs-CRP ($P < .0001$), IL-18 ($P < .0001$), and IL-6 ($P < .0001$) (Table 2).

Table 3
Multiple regression analysis results with the inflammatory factors and *M* value as independent variables and the components of MS and total NCEP score as dependent variables

	Waist	SBP	DBP	Glucose	TG	HDL cholesterol	Total score
IL-18	$\beta = .19$, $P = .0019$	$\beta = .11$, $P = .11$	$\beta = .11$, $P = .11$	$\beta = .11$, $P = .09$	$\beta = .27$, $P = .000017$	$\beta = -.13$, $P = .05$	$\beta = .16$, $P = .0082$
M	$\beta = -.45$, $P < .000001$	$\beta = -.22$, $P = .0013$	$\beta = -.25$, $P = .00042$	$\beta = -.38$, $P < .000001$	$\beta = -.39$, $P < .000001$	$\beta = .33$, $P = .000001$	$\beta = -.52$, $P < .000001$
Adiponectin	$\beta = -.37$, $P < .000001$	$\beta = -.23$, $P = .0014$	$\beta = -.20$, $P = .0047$	$\beta = -.15$, $P = .032$	$\beta = -.19$, $P = .001$	$\beta = .19$, $P = .0063$	$\beta = -.23$, $P = .00029$
M	$\beta = -.39$, $P < .000001$	$\beta = -.16$, $P = .023$	$\beta = -.20$, $P = .0061$	$\beta = -.30$, $P = .000019$	$\beta = -.34$, $P = .000001$	$\beta = -.28$, $P = .000066$	$\beta = -.46$, $P < .000001$
IL-6	$\beta = .20$, $P = .00062$	$\beta = -.02$, $P = .79$	$\beta = .03$, $P = .65$	$\beta = .15$, $P = .016$	$\beta = .05$, $P = .44$	$\beta = -.17$, $P = .0096$	$\beta = .21$, $P = .00028$
M	$\beta = -.47$, $P < .000001$	$\beta = -.27$, $P = .00011$	$\beta = -.27$, $P = .00008$	$\beta = -.38$, $P < .000001$	$\beta = -.46$, $P < .000001$	$\beta = .33$, $P = .000001$	$\beta = -.52$, $P < .000001$
Hs-CRP	$\beta = .37$, $P = .000033$	$\beta = -.11$, $P = .26$	$\beta = -.02$, $P = .83$	$\beta = .26$, $P = .0058$	$\beta = .09$, $P = .30$	$\beta = -.23$, $P = .014$	$\beta = .32$, $P = .00019$
M	$\beta = -.23$, $P = .0077$	$\beta = -.22$, $P = .027$	$\beta = -.25$, $P = .012$	$\beta = -.16$, $P = .09$	$\beta = -.37$, $P = .000087$	$\beta = .21$, $P = .029$	$\beta = -.36$, $P = .000023$
sTNFR1	$\beta = .28$, $P = .000005$	$\beta = .13$, $P = .069$	$\beta = .10$, $P = .14$	$\beta = .22$, $P = .00063$	$\beta = .29$, $P = .000003$	$\beta = -.14$, $P = .04$	$\beta = .22$, $P = .00022$
M	$\beta = -.44$, $P < .000001$	$\beta = -.24$, $P = .00061$	$\beta = -.26$, $P = .00018$	$\beta = -.34$, $P < .000001$	$\beta = -.39$, $P < .000001$	$\beta = .33$, $P = .000002$	$\beta = -.51$, $P < .000001$
sTNFR2	$\beta = .28$, $P < .000001$	$\beta = .06$, $P = .33$	$\beta = .05$, $P = .43$	$\beta = .14$, $P = .023$	$\beta = .19$, $P = .0014$	$\beta = -.24$, $P = .0002$	$\beta = .24$, $P = .000014$
M	$\beta = -.49$, $P < .000001$	$\beta = -.27$, $P = .000055$	$\beta = -.29$, $P = .000019$	$\beta = -.39$, $P < 0.000001$	$\beta = -.46$, $P < .000001$	$\beta = .34$, $P < .000001$	$\beta = -.55$, $P < .000001$

The correlation analysis showed inverse relationships between the number of NCEP criteria and insulin sensitivity ($r = -0.57$, $P < .0001$) and adiponectin ($r = -0.37$, $P < .0001$) (Fig. 1), and positive correlations with fasting insulin ($r = 0.52$, $P < .0001$), postload insulin ($r = 0.53$, $P < .0001$), sTNFR1 ($r = 0.38$, $P < .0001$), sTNFR2 ($r = 0.31$, $P < .0001$), IL-18 ($r = 0.31$, $P < .0001$), IL-6 ($r = 0.33$, $P < .0001$) (Fig. 1), and hs-CRP ($r = 0.47$, $P < .0001$).

In the multiple regression analysis, we observed that adiponectin and inflammatory factors (IL-18, IL-6, hs-CRP, sTNFR1, and sTNFR2) predicted NCEP score independent of insulin sensitivity (all adjusted β values between .16 and .32, all Ps < .01; Table 3). This was attributed mostly to independent associations with individual components of MS —adiponectin was related to all its components (adjusted β values between −.15 and −.37, all Ps < .05), whereas proinflammatory proteins were related to waist, glucose (except IL-18), TG (except IL-6 and hs-CRP), and HDL cholesterol (all adjusted β values between .15 and .37, all Ps < .05; Table 3).

All findings observed in the entire group were still significant in the group of subjects with normal glucose tolerance (data not shown).

4. Discussion

The present study performed in a young adult population with a wide range of BMI revealed that about 20% fulfilled the criteria for MS. In agreement with previous observations, subjects with MS were older and more obese than the subjects without MS [1].

All studied proinflammatory cytokines were markedly elevated in the subjects with MS. Similar observations were previously reported by different group of researchers for single proteins like IL-18 [23], sTNFR1 [24], and CRP [8]. Furthermore, Salmenniemi and coauthors [25] proved an increase in CRP, IL-6, and other cardiovascular risk markers in individuals with MS, although the criteria for diagnosis of MS were different from the NCEP score used in this study. The above findings were accompanied by a decrease in serum adiponectin concentration. This is in agreement with the aforementioned studies reporting hypoadiponectinemia in obesity, insulin resistance, and type 2 diabetes mellitus. Ryo et al [26] suggested that hypoadiponectinemia could be a useful biomarker for MS. In our study, serum adiponectin decreased concurrently with an increased number of components of NCEP score. In addition, insulin sensitivity, estimated by the clamp study, decreased with an increase in the number of fulfilled MS criteria. In most studies concerning MS and insulin resistance, only indirect estimates of insulin sensitivity were used [14]. However, close association of MS with insulin resistance was apparent when the clamp [27], minimal model analysis [28], or insulin suppression test [29] was used. In these studies, the sensitivity of NCEP criteria to identify the subjects with insulin resistance was low. Our study, however, was not designed to solve this problem.

If we look for a single component of MS complying with NCEP criteria, the most common, in our young population, was the waist circumference, which indicates the significance of visceral fat accumulation in the pathogenesis of MS. Carr et al [30] demonstrated that intraabdominal fat, assessed by computed tomography, is the major determinant of NCEP-defined MS through independent relationships with all its components. Opposing results were obtained in the study of Saely et al [31]. In a big group of 736 patients undergoing coronary arteriography, the waist circumference criterion was present only in 50% of individuals with MS [31]. It points out the role of study group characteristics in the context of concomitant disorders [31] and ethnicity [32].

In our study, the results of multiple regression analysis show that inflammation and insulin resistance are associated with the total NCEP score independent of each other. The same was also observed for particular components of MS. Interestingly, separate adipocytokines were differently related to particular NCEP criteria. We should underline that, in our population, adiponectin was independently related to all components of MS. The present study does not show any cause-effect relationship. Our findings could suggest that the association of inflammation with MS exceeds its relation with insulin resistance. If we take into account that body fat accumulation leads to insulin resistance, hypoadiponectinemia, and up-regulation of proinflammatory factors, we might hypothesize that obesity can be a factor inducing the above abnormalities, which together are responsible for development of MS. In our study, this idea is supported by the fact that only 4 subjects with MS did not fulfill the waist criterion. It was already indicated by Reaven [33] that obesity plays rather a causative role in the development of insulin resistance, in contrast to other components of MS, which might be in part a consequence of insulin resistance.

The population examined in the present study was much younger than those reported in the literature by other researches in adults [34]. Our findings indicate that MS, even if it is present relatively early in the adult life, is associated with inflammatory abnormalities and insulin resistance in a degree comparable with the older population. It points out the necessity of early prevention of cardiovascular complications.

We conclude that young subjects with MS demonstrate, regardless of insulin resistance, an increased inflammatory response and lower adiponectin concentration.

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