Core and concomitant components of the metabolic syndrome according to their relation to the insulin resistance indexes in patients with suspected metabolic syndrome

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Summary

Objectives: We sought to analyze what are the core components of the metabolic syndrome and which cardiovascular risk factors are concomitant according to their relation to the insulin resistance indexes.

Methods: We studied 127 subjects (64% of men and 36% of women, aged 49.8 ± 9.4 years) suspected to have metabolic syndrome (MS). All the patients underwent detailed assessment of cardiovascular risk factors, including a serum lipid profile measurement and an oral glucose tolerance test (OGTT). Serum insulin was measured at baseline and 120 minutes after the glucose load. Insulin resistance indexes $HOMA_{IR}$ and ISI were calculated.

Results: The metabolic syndrome according to the National Cholesterol Education Program (NCEP) Adult Treatment Panel (ATP) III was diagnosed in 55 patients (43%). Majority of the study patients ($n = 113$, 89%) had central obesity as described by the International Diabetes Federation (IDF) criteria. Therefore, the MS according to the IDF was found in more than half of the patients ($n = 83$, 65%). Newly diagnosed diabetes, impaired glucose tolerance or fasting hyperglycaemia was present in 84 patients (66%). Normal fasting glucose (<5.6 mmol/l) had 39% of patients with impaired glucose tolerance ($n = 9$ out of 23). Typical for the metabolic syndrome dyslipidemia according to the IDF criteria was found in 70 patients (55%). Any type of dyslipidemia was present in 91 patients (72%).

Insulin resistance indexes ($HOMA_{IR}$ and ISI) were correlated with body mass index ($r = 0.36$, $p < 0.0001$ and $r = –0.321$, $p = 0.003$, respectively) and waist circumference ($r = 0.40$, $p < 0.0001$ for $HOMA_{IR}$; $r = –0.31$, $p = 0.004$ for ISI), as well as with fasting and OGTT glycaemia (for fasting glycaemia $r = 0.48$, $p < 0.001$ and $r = –0.33$, $p = 0.002$, respectively). No relationship was found between insulin resistance indexes and the presence of arterial hypertension (logistic regression coefficient $\beta = 0.17$, $p = 0.52$ for $HOMA_{IR}$ and $\beta = –1.23$, $p = 0.34$ for ISI). Correlation between insulin resistance indexes ($HOMA_{IR}$, ISI) and serum lipid profile was not found as well.

Conclusions: Central obesity and any type of glycaemic disorder seem to be the core components of the metabolic syndrome. Waist circumference as a marker of central obesity is significantly correlated with the insulin resistance indexes. An oral glucose tolerance test next to the estimation of fasting glucose gives additional value for discrimination of subjects with glycaemic disorder.

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Type 2 diabetes and cardiovascular diseases share common metabolic risk factors: abdominal obesity, glycaemic disorder, dyslipidemia and arterial hypertension that are joined to the so-called metabolic syndrome [1]. The metabolic syndrome (MS) is related to high morbidity and mortality rates. Although it is one of the most powerful predictors of cardiovascular events, the definition of the metabolic syndrome is still under formation.

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Several definitions of the metabolic syndrome have been proposed over the past seven years. They differ in regard to the key component of the syndrome, the list of components or their definitions.

The World Heart Organization (WHO) in 1999 issued guidelines for the diagnosis of metabolic syndrome [1]. According to them, the necessary component of the metabolic syndrome should be a disorder of glucose metabolism defined as diabetes mellitus (DM), impaired glucose tolerance (IGT), fasting hyperglycaemia (FH) or insulin resistance. Additionally, the presence of at least two other components from the list of four: arterial hypertension (treated or blood pressure higher than 160/90 mm Hg), typical dyslipidemia (serum tryglicerides $\geq$1.7 mmol/l and/or HDL-cholesterol $\leq$0.9 mmol/l in males and $\leq$1.0 in females), obesity (body mass index $\geq$30 kg/m^2 or waist-hip ratio >0.90 in males and >0.85 in females) and microalbuminuria was required.

The National Cholesterol Education Program (NCEP) Expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (Adult Treatment Panel III, ATPIII) proposed a different model of the metabolic syndrome [2]. Based on the attitude that all underlying components of the metabolic syndrome are interrelated, this model does not exclude any key components but requires the presence of at least three of the following symptoms: central obesity (waist circumference >102 cm in males and >88 cm in females), triglycerides $\geq$1.7 mmol/l, HDL-cholesterol $\leq$1 mmol/l in males and $\leq$1.3 in females, arterial blood pressure higher than or equal to 130/85 mm Hg, fasting glucose $\geq$6.1 mmol/l. This definition underlines the importance of central obesity vs the elevation of body mass index, linking it with the insulin resistance, and sets a lower cut-off point for arterial hypertension.

On April 14, 2005 the International Diabetes Federation (IDF) issued a consensus statement presenting a new definition of the metabolic syndrome [3]. The essential component in this definition is central obesity with the ethnicity-specific and lower waist girth levels than the ATP III definition: in Europids it is defined as a waist equal to or more than 94 cm for males and 80 cm for females. Central obesity should be accompanied by at least two of the following symptoms: raised triglycerides of at least 1.7 mmol/l; low HDL-cholesterol defined as less than 1.04 mmol/l in males and less than 1.29 mmol/l in females; raised blood pressure of at least 130/85 mm Hg; fasting hyperglycaemia, previous diagnosis of type 2 diabetes. The IDF adopted the American Diabetes Association (ADA)-suggested level for impaired fasting glucose (IFG) equal to or greater than 5.6 mmol/l.

With not yet longitudinal studies using new criteria conducted, the question of the best definition of the metabolic syndrome is still open. Since insulin resistance measures are considered to play a key role in the development of cardiovascular diseases, careful evaluation of components of the metabolic syndrome in relation to insulin resistance indexes is needed. That would help to estimate the core and concomitant components of the metabolic syndrome.

Therefore the purpose of our study was to analyze what are the core components of the metabolic syndrome and what risk factors are concomitant according to their relation to the insulin resistance indexes.

Design and methods

Study design

A cross-sectional study design was applied. The study was performed at Vilnius University Hospital Santariškių Klinikos within 2001–2003. Subjects under 65 years old referred to the Preventive Cardiovascular Care Unit or recruited from the hospital staff because of at least two signs of the metabolic syndrome (according to the NCEP ATP III or the World Health Organization criteria) present were included into the study. Initially we collected data of 288 patients with suspected metabolic syndrome. After primary evaluation patients on lipid lowering drugs or with lipid lowering treatment less than 3 months prior to the clinical assessment were excluded. Only 127 patients without cholesterol lowering treatment were included into the study. Patients receiving other cardiovascular drugs for the treatment of coronary heart disease and arterial hypertension were not excluded. The study was approved by the local ethics committee.

All the patients underwent detailed assessment of cardiovascular risk factors. Initially medical history data were collected and anthropometric measurements were carried out. After at least 12 hours of the fasting period, blood samples for the serum lipid profile were drawn and the oral glucose tolerance test (OGTT) was performed. Serum insulin was measured at baseline and 120 minutes after the glucose load. The homeostatic insulin resistance model ($HOMA_{IR}$) score and the Insulin Sensitivity Index (ISI) according to the M Matsuda formula [4,5] were calculated in order to evaluate insulin resistance:

$$HOMA_{IR} = \left[insulin_{fasting}\ (\mu IU/ml) \times glucose_{fasting}\ (mmol/l)\right]/22.5,$$

$$ISI = 10\,000/sqrt(insulin_{fasting} \times glucose_{fasting} \times insulin_{OGTT} \times glucose_{OGTT}).$$

The presence of metabolic syndrome and relationships of various components of the metabolic syndrome were analyzed by applying both the IDF and the ATP III classifications.

The study conforms to the principles outlined in the Declaration of Helsinki.

Statistical analysis

Data are expressed as mean ± SD or as counts (n) and percentages. When comparing two groups, the Student t test was performed for continuous variables. For the comparison of nonparametric data chi-square (χ^2) analysis was applied. Pearson correlation analysis was performed in order to establish correlation between parametric variables. Multivariate analysis using a logistic regression model was used to analyze the relationship of binary variables such as the presence of arterial hypertension with other components of the metabolic syndrome, expressed as continues variables. Statistical analysis was performed using Statistica for Windows V.5.0.

Results

Background of the study population

We studied 127 subjects – 81 men (64%) and 46 women (36%), aged 49.8 ± 9.4 years suspected to have MS. All the patients had at least two signs of the metabolic syndrome described by the WHO or the NCEP ATP III criteria. Main characteristics of the patients are presented in Tables 1–3.

Less than one half of the study patients ($n = 60$, 47%) were diagnosed with coronary heart disease and majority of the study population ($n = 114$, 90%) – with arterial hypertension. Nevertheless, only a part of all the patients received appropriate treatment prior to cardiovascular assessment: 59 patients (46%) were treated with aspirin, 61 patients (48%) – with beta-blockers, 47 patients (37%) – with angiotensin converting enzyme inhibitors, 35 patients (28%) – with calcium channel blockers, 16 patients (13%) – with diuretics, 7 patients (5%) – with other antihypertensive drugs. More than half of hypertensive patients ($n = 72$, 63%) were drug-naive before the initial assessment. Although 91 patients (72%) had dyslipidemia, there were no study patients on statins or other lipid-lowering treatment due to the ini-

Table 1.
Characteristics of the study patients

	N (%) or mean ± SD
Number of patients	127 (100%)
Male patients	81/46 (64/36%)
Age, years	49.8 ± 9.4
Height	173.4 ± 10.3
Weight, kg	95.2 ± 16.5
BMI, kg/m^2	31.4 ± 5.5
BMI > 25 kg/m^2	120 (94%)
Waist circumference, cm	105.0 ± 11.1
Patients with central obesity according to IDF	113 (89%)
Patients with central obesity according to ATP III	80 (63%)
Arterial hypertension	114 (90%)
Coronary heart disease	60 (47%)
Dyslipidemia	91 (72%)
Typical for MS dyslipidemia according to IDF*	70 (55%)
Typical for MS dyslipidemia according to ATP III**	62 (49%)
Impaired glucose tolerance	23 (18%)
Diabetes mellitus	7 (5%)
Fasting hyperglycaemia according to IDF	75 (59%)
Fasting hyperglycaemia according to ATP III	37 (29%)
Any glycaemic disorder	84 (66%)

ATP – Adult Treatment Panel; BMI – body mass index; IDF – International Diabetes Federation; MS – metabolic syndrome.
* Typical dyslipidemia, according to IDF – raised triglycerides of at least 1.7 mmol/l and/or low high-density lipoprotein cholesterol, defined as less than 1.04 mmol/l in males and less than 1.29 mmol/l in females; ** Typical dyslipidemia, according to ATP III – raised triglycerides of at least 1.7 mmol/l and/or low high-density lipoprotein cholesterol, defined as less than 1.00 mmol/l in males and less than 1.3 mmol/l in females.

Table 2.
Characteristics of the patients with central obesity according to the International Diabetes Federation criteria

	N (%) or mean ± SD
Number of patients	113 (100%)
Male patients	69/44 (61/49%)
Age, years	50.3 ± 8.8
Height	173.0 ± 10.7
Weight, kg	95.7 ± 16.8
BMI, kg/m^2	31.9 ± 4.8
Waist circumference, cm	105.5 ± 11.1
Arterial hypertension	99 (88%)
Coronary heart disease	55 (49%)
Dyslipidemia	82 (73%)
Typical for MS dyslipidemia*	64 (57%)
Impaired glucose tolerance	22 (20%)
Diabetes mellitus	6 (5%)
Fasting hyperglycaemia	57 (50%)
Any glycaemic disorder	73 (65%)

BMI – body mass index; MS – metabolic syndrome.

Table 3.
Laboratory findings in study patients

	All patients, mean ± SD	Patients with CO according to IDF, mean ± SD
Total cholesterol, mmol/l	6.3 ± 1.4	6.2 ± 1.4
LDL-cholesterol, mmol/l	4.0 ± 1.3	4.0 ± 1.3
HDL-cholesterol, mmol/l	1.3 ± 0.3	1.3 ± 0.3
Tryglicerides, mmol/l	2.1 ± 1.9	2.2 ± 2.1
Fasting serum glucose	5.7 ± 0.7	5.7 ± 0.7
Serum glucose after 120 minutes	6.4 ± 2.4	6.4 ± 2.4
Fasting insulin	12.3 ± 5.8	12.4 ± 5.6
Serum insulin after 120 minutes	50.2 ± 46.9	51.1 ± 46.9
$HOMA_{IR}$	3.2 ± 1.7	3.2 ± 1.7
ISI	111.9 ± 81.5	109.6 ± 81.2

CO – central obesity according to International Diabetes Federation; HDL – high-density lipoprotein; $HOMA_{IR}$, ISI – insulin sensitivity indexes; IDF – International Diabetes Federation; LDL – low-density lipoprotein.

tial exclusion. All patients with glyceamic disorders were newly diagnosed and not yet treated.

Frequency of the components of the metabolic syndrome

The average body mass index (BMI) in the study patients was elevated up to 31.4 ± 5.5 kg/m^2. BMI exceeding 25 was present in 120 patients (90%). Majority of the patients ($n = 113$, 89%) had central obesity according to the International Diabetes Federation (IDF) criteria as waist circumference equal to or more than 94 cm for males and 80 cm for females. When the ATP III criteria were applied, only 84 patients (66%) were diagnosed with central obesity. 110 patients (92%) with central obesity had elevated BMI (more than 25 kg/m^2).

Abnormal glucose metabolism (fasting hyperglycaemia according to the IDF criteria, the presence of diabetes mellitus or impaired glucose tolerance) was found in more than half of the study patients ($n = 84$, 66%). Fasting hyperglycaemia at least 5.6 mmol/l was found in 75 patients (59%), impaired glucose tolerance according to the OGTT – in 23 patients (18%). More than one third of 23 patients with impaired glucose tolerance ($n = 9$, 39%) had normal fasting glucose (<5.6 mmol/l), 14 patients had both – elevated fasting glucose and impaired glucose tolerance. Newly diagnosed diabetes was observed in 7 patients (5%). When the ATP III criteria were applied fasting hyperglycaemia was diagnosed in significantly lower frequency as compared to the results obtained by applying the IDF criteria – 37 patients (29%) vs 75 patients (59%), $p < 0.05$. Central obesity according to the IDF was present in 63 (75%) of these patients; 70 (83%) of them had elevated BMI and only one patient had glycaemic disorder without any type of obesity.

Arterial hypertension (the definitions were the same both for the ATP III and the IDF classifications) was found in 113 subjects (89%) – 74 men and 39 women.

Any type of dyslipidemia was found in 91 patients (72%). Mean total cholesterol, low density lipoprotein (LDL) cholesterol and tryglicerіde levels were elevated (6.3 ± 1.4 mmol/l, 4.0 ± 1.3 mmol/l and 2.1 ± 1.9 mmol/l, respectively), although mean high density lipoprotein (HDL) cholesterol was quite high – 1.3 ± 0.3 mmol/l. Typical for the metabolic syndrome dyslipidemia defined by the IDF criteria (raised triglycerides of at least 1.7 mmol/l and/or low HDL-cholesterol, defined as less than 1.04 mmol/l in males and less than 1.29 mmol/l in females) was present only in 70 patients (55%).

The metabolic syndrome according to the IDF criteria was found in 83 patients (65%). Only 9 (8%) of obese patients had all five components of the MS. In the majority of cases ($n = 74$, 89%) obese patients had at least two of the four other signs of the MS and only 5 patients (6%) had isolated central obesity without other abnormalities typical for the MS (Table 4).

The metabolic syndrome as defined by ATP III was diagnosed in 55 patients (43%). Five components of the MS had 7 patients (6%). More than half of obese patients had at least two of the four other signs of the MS ($n = 49$, 58%). Only 6 (11%) of the patients diagnosed with the MS according to ATP III had other than central obesity signs of the metabolic syndrome (Table 4).

Hence, metabolic syndrome defined by the IDF criteria was found in 83 patients (65%) and only 55 patients (43%) were diagnosed with the MS when applying the ATP III criteria. Totally in 86 patients (68%) the MS could be found using either one or another classification.

Table 4.
Distribution of components of metabolic syndrome according to the International Diabetes Federation and Adult Treatment Panel III definitions

Components of MS	Number (%) of patients according to	
	IDF criteria	ATP III criteria
CO and 4 other components	**9** (**7.1**)	**7** (**5.5**)
CO and 3 other components:	**29** (**22.8**)	**23** (**18.1**)
TG + gl + AH	19 (15.0)	14 (11)
HDL + AH + gl	6 (4.7)	4 (3.1)
TG + HDL + AH	4 (3.1)	5 (3.9)
CO and 2 other components:	**45** (**35.4**)	**19** (**15.0**)
gl + TG	3 (2.4)	0
AH + gl	25 (19.7)	9 (7.1)
AH + TG	11 (8.7)	6 (4.7)
AH + HDL	4 (3.1)	4 (3.1)
CO and 1 other component:	**25** (**19.7**)	**28** (**22.0**)
AH	20 (15.7)	24 (18.9)
HDL	1 (0.8)	0 (0)
TG	1 (0.8)	3 (2.4)
gl	2 (1.6)	1 (0.8)
CO only	**5** (**3.9**)	**3** (**2.4**)
Other than CO components	**14** (**11.0**)	**47** (**37.0**)
MS without CO*	–	**6** (**4.7**)
Totally:	**127** (**100.0**)	**127** (**100.0**)
Patients with metabolic syndrome	**83** (**65.4**)	**55** (**43.0**)
Patients without metabolic syndrome	**44** (**34.6**)	**72** (**57.0**)

* Calculation only for metabolic syndrome according Adult Treatment Panel III criteria. AH – arterial hypertension; ATP – Adult Treatment Panel; CO – central obesity; gl – glycaemic disorder; HDL – low high-density lipoprotein cholesterol; IDF – International Diabetes Federation; MS – metabolic syndrome; TG – elevated triglycerides.

Table 5.
Relationship of the insulin resistance indexes with other components of the metabolic syndrome

Parameters	HOMA-IR	ISI
Fasting glucose, mmol/l	**$r = 0.48$, $p < 0.001$**	**$r = -0.33$, $p = 0.02$**
OGTT serum glucose after 120 minutes	**$r = 0.34$, $p = 0.001$**	**$r = -0.69$, $p < 0.001$**
Fasting serum insulin, μIU/ml	**$r = 0.97$, $p < 0.001$**	**$r = -0.60$, $p < 0.01$**
OGTT serum insulin after 120 minutes, μIU/ml	**$r = 0.51$, $p < 0.01$**	**$r = -0.62$, $p < 0.001$**
Total cholesterol, mmol/l	$r = -0.16$, $p = 0.16$	$r = -0.005$, $p = 0.97$
LDL-Ch, mmol/l	$r = 0.07$, $p = 0.55$	$r = -0.09$, $p = 0.42$
HDL-Ch, mmol/l	$r = -0.05$, $p = -0.66$	$r = -0.06$, $p = 0.61$
Triglycerides, mmol/l	$r = 0.08$, $p = 0.45$	$r = -0.05$, $p = 0.67$
BMI, kg/m^2	**$r = 0.36$, $p < 0.001$**	**$r = -0.321$, $p = 0.003$**
Waist circumference, cm	**$r = 0.40$, $p < 0.001$**	**$r = -0.31$, $p = 0.004$**
Arterial hypertension	$\beta = 1.18$, $p = 0.52$	$\beta = 0.29$, $p = 0.34$

BMI – body mass index; HDL – high-density lipoprotein cholesterol; $HOMA_{IR}$, ISI – insulin sensitivity indexes; LDL-Ch – low-density lipoprotein cholesterol; OGTT – oral glucose tolerance test; p – p-value; r – Pearson correlation coefficient; β – logistic regression coefficient.

Relationship of metabolic syndrome components to insulin resistance indexes

Insulin resistance indexes ($HOMA_{IR}$ and ISI) were correlated with fasting as well as OGTT serum glucose and insulin levels (Table 5).

Significant correlation of insulin resistance indexes ($HOMA_{IR}$ and ISI) with body mass index ($r = 0.36$, $p < 0.0001$ and $r = -0.321$, $p = 0.003$, respectively) as well as with waist circumference ($r = 0.40$, $p < 0.0001$ for $HOMA_{IR}$; $r = -0.31$, $p = 0.004$

Table 6.
Serum glucose and insulin changes during oral glucose tolerance test: comparison of obese vs non-obese patients (according to the Adult Treatment Panel III definition of central obesity)

Glycaemic parameter	Patients without CO, mean ± SD	Patients with CO, mean ± SD	*p*-value
Fasting glucose, mmol/l	5.69 ± 0.71	5.78 ± 0.75	0.52
OGTT serum glucose after 120 minutes	5.89 ± 2.27	6.72 ± 2.44	0.06
Fasting serum insulin, μIU/ml	10.26 ± 5.19	13.32 ± 5.79	**0.01**
OGTT serum insulin after 120 minutes, μIU/ml	55.40 ± 86.39	54.34 ± 48.75	0.94

CO – central obesity, OGTT – oral glucose tolerance test.

for ISI) was found. Interestingly, the correlation between insulin resistance indexes ($HOMA_{IR}$ and ISI) and waist circumference ($r = 0.40$, $p < 0.001$ and $r = -0.31$, $p = 0.004$, respectively) was very close to the correlation between these indexes and fasting glucose ($r = 0.48$, $p < 0.001$ and $r = -0.33$, $p = 0.002$, respectively) thus confirming the importance of central obesity in the prediction of insulin resistance.

When IDF criteria were applied, no significant difference of insulin resistance measures between two subgroups – in patients with central obesity and without central obesity was observed ($HOMA_{IR}$ 3.03 ± 1.68 vs 3.19 ± 1.69, $p = 0.76$ and ISI 137.69 ± 86.91 vs 109.57 ± 81.22, $p = 0.38$, respectively). Furthermore, there was no statistically significant difference in the frequency of insulin resistance between obese patients (waist circumference >94 cm for males and >80 cm for females) and lean patients: 21% ($n = 26$) obese patients vs 14% ($n = 2$) patients without obesity had insulin resistance defined as $HOMA_{IR} \geq 4$ ($\chi^2 = 0.26$, Fisher exact $p = 0.46$).

However, when central obesity was defined according to the ATP III criteria (waist circumference >102 cm for males and >88 cm for females), statistically significant differences were found. Patients with central obesity as compared to patients without this condition had higher $HOMA_{IR}$ and lower ISI indexes ($HOMA_{IR}$ 3.47 ± 1.78 vs 2.59 ± 1.27, $p = 0.01$; ISI 100.11 ± 70.72 vs 137.52 ± 97.86, $p = 0.04$). Insulin resistance was more common in obese patients ($n = 22$ out of 84) as compared to non-obese ($n = 4$ out of 43) – 27% vs 9%, respectively ($\chi^2 = 3.46$, Fisher exact $p = 0.047$).

No relationship was found between insulin resistance indexes and the presence of arterial hypertension (logistic regression coefficient $\beta = 0.17$, $p = 0.52$ for $HOMA_{IR}$ and $\beta = -1.23$, $p = 0.34$ for ISI).

Correlation between the serum lipid profile and $HOMA_{IR}$ as well as ISI was not found as well (Table 5).

Discussion

People with metabolic syndrome are at increased risk for diabetes and cardiovascular disease [6–8]. Several classifications are proposed for the definition of the metabolic syndrome: the World Heart Organization, NCEP/ATP III and recently the International Diabetes Federation consensus statement [1–3]. It is difficult yet to estimate the real prevalence of the metabolic syndrome in the population worldwide because of the existing difference in definitions. Switching from one definition to another leads to different rates of prevalence of the metabolic syndrome in population. The prevalence of the metabolic syndrome using the NCEP/ATP III criteria among the US adults was 21.7% during 1988–1994 [9], it ranged from 21.3 to 32.8% among participants of the Framingham Offspring Study and the San Antonio Heart Study during the early to mid-1990s [10]. In the National Health and Nutrition Examination Survey (NHANES) conducted lately in 1999–2002, the unadjusted prevalence of the metabolic syndrome according to the NCEP definition, was 34.5 ± 0.9% (percent ± SE) among all participants, 33.7 ± 1.6% among men, and 35.4 ± 1.2% among women; based on the IDF definition, it was 39.0 ± 1.1% among all participants, 39.9 ± 1.7% among men, and 38.1 ± 1.2% among women [11]. Hence, the use of the IDF classification in the USA leads to a higher prevalence estimate of the metabolic syndrome than the estimate based on the NCEP definition [11]. Although it was stated that the IDF classification is proposed for the harmonization of situation all over the world, it requires a reassessment of the prevalence of the metabolic syndrome as well as of the magnitude of the morbidity and mortality associated with the metabolic syndrome. There is a fundamental difference in terms of core components of the metabolic syndrome between the classifications. Switching from glycaemic disorders in the NCEP classification to central obesity in the IDF is the most prominent change.

The main purpose of our study was to analyze what could be the core components of the metabolic syndrome based on the resistance to insulin as the main mechanism of this syndrome.

We measured the indirect insulin resistance indexes ($HOMA_{IR}$ and ISI). The Homeostasis Model Assessment ($HOMA_{IR}$) method developed by Matthews et al includes measurements of insulin sensitivity from fasting serum insulin and fasting plasma glucose [4]. The insulin sensitivity indices (ISI) method developed by Matsuda and DeFronzo anticipates the measurements obtained from the oral glucose tolerance testing [5]. The close relationship of this measurement with direct measurements of insulin resistance by the euglycaemic insulin clamp was demonstrated [5]. The OGTT is in part determined by sensitivity of peripheral tissues to insulin. Therefore, the OGTT has been used by us in all patients and indices of the insulin sensitivity have been derived from two measurements of serum insulin and glucose (at baseline and 120 minutes after the glucose load).

We were able to show that $HOMA_{IR}$ and ISI were correlated closely with body mass index and waist circumference. Interestingly, the correlation between insulin resistance indexes and waist circumference was very close to the correlation between these indexes and fasting glucose thus confirming the reliability of central obesity as the core component in prediction of insulin resistance. That favors the use of the IDF classification with the main role of central obesity in it. But in our study we demonstrated that when strict IDF criteria of abdominal obesity were applied, no significant difference of insulin resistance measures between two subgroups – in patients with central obesity and without central obesity was observed. Furthermore there was no statistically significant difference in the frequency of insulin resistance between obese patients (waist circumference >94 cm for males and >80 cm for females) and lean patients. However, when central obesity was defined according to the ATP III criteria (waist circumference >102 cm for males and >88 cm for females), statistically significant differences were found. It makes us doubtful if the Europoid men and women criteria of obesity (defined as waist circumference $\geq$94 cm for men and $\geq$80 cm for women) should be applicable for our Lithuanian population.

Debatable seems also the decision to consider the impaired fasting glucose as the secondary (next to central obesity) component of metabolic syndrome in the IDF classification [3]. From one side in our study we could reveal the close correlation of insulin resistance with fasting glucose. From another – fasting glucose was not enough sensitive for initial diagnosis of the MS in early stages of pathology. The use of elevated fasting glucose alone as a parameter of the glycaemic disorder was already the problem in the NCEP classification. That could be the reason why in 2003 the American Diabetes Association (ADA) reduced the cut-point for impaired fasting glucose from 6.1 to 5.6 mmol/l and introduced the term “prediabetic” in the USA [12]. This term is unfortunate since it presumes that such people will become diabetic, but there is no prospective data to support such a statement [13]. More logical would seem in the subjects under the suspicion of the metabolic syndrome but with normal fasting glucose to perform an oral glucose tolerance test. By the way, that was recommended in the WHO classification [1]. According to our results 39% of patients with the suspected metabolic syndrome had impaired glucose tolerance but normal fasting glucose (<5.6 mmol/l). May be the subjects with impaired glucose tolerance and abnormal response to the oral glucose load differ in terms of mechanisms responsible for the metabolic syndrome from those with constantly elevated fasting glucose. Other studies also show the oral glucose tolerance test to be a more sensitive method [14–16].

Consequently, our study revealed two core components of the metabolic syndrome – central obesity and/or any form of the glycaemic disorder. Other components – specific lipid profile (elevated triglycerides and/or lowered high-density lipoprotein) and hypertension are next to these main components. Such statement could be supported by the results of our study. According to the logistic regression analysis there was no relationship between insulin resistance indexes and the presence of arterial hypertension in our study. However, careful interpretation of this result should be applied in order to prevent misleading conclusions for the high prevalence of arterial hypertension in our study. Arterial hypertension was observed in majority of our study patients ($n = 114$, 90%). The correlation between the serum lipid profile and insulin resistance indexes $HOMA_{IR}$ and ISI was not found as well. Moreover, typical for the metabolic syndrome form of the lipid profile was present only in 55% of patients in our study and any type of dyslipidemia was present in 72% of patients with metabolic syndrome. Therefore, in our everyday clinical practice we would prefer to speak about the arterial hypertension next to the metabolic syndrome (arterial hypertension with metabolic syndrome) or dyslipidemia next to the metabolic syndrome (dyslipidemia with metabolic syndrome).

The possible effect of antihypertensive and antiischemic drug treatment to the serum lipid and glucose parameters also should be taken into consideration. However, all patients received latest generation drugs with a little possible metabolic effect and there were no patients on statins and other lipid lowering drugs or antiglycaemic treatment.

The story with the metabolic syndrome definition is not yet finished. Insulin resistance indexes next to the fasting glycaemia and an oral glucose loading test should be used in everyday clinical practice for the precise measurement of the glycaemic disorder [17]. Further studies must be addressed to the study of clinical significance of the loss of early insulin secretion and peak glycaemic response to an oral glucose load additionally to the evaluation of fasting glucose and glycaemia 2 hours after the glucose load [18]. The evolving criteria of the metabolic syndrome: C-reactive protein, adiponectin level, endothelial dysfunction are studied intensively [19–22].

Conclusions

Central obesity and any type of glycaemic disorder seem to be the core components of the metabolic syndrome. Waist circumference as a marker of central obesity is significantly correlating with the insulin resistance indexes. Strict cut-off points of the IDF criteria for central obesity are less sensitive to discriminate between patients with insulin resistance and without it as compared to the criteria of NCEP ATP III. An oral glucose tolerance test next to the estimation of fasting glucose gives additional value for the discrimination of subjects with glycaemic disorder. So-called typical or atypical dyslipidemia and arterial hypertension could be considered as next to the core metabolic syndrome components existing cardiovascular risk factors. The more flexible approach for the classification of the metabolic syndrome is needed for everyday clinical practice.

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