International Heart and Vascular Disease Journal
Volume 5, Number 15, September 2017

Journal of the Cardioprogress Foundation

Clinical and biochemical features of the metabolic syndrome in men

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Summary

Objective

To reveal clinical and biochemical particularities of the metabolic syndrome in men.

Materials and methods

The study included 299 men with metabolic syndrome aged from 31 to 89 years.

Results

We identified the presence of hypertriglyceridemia and increased quantity of low density lipids in young males, whereas carbohydrate metabolism disorders prevailed in middle-aged men. In 52% of cases metabolic syndrome was combined with overweight. The body mass index was significantly higher in men with manifestation of obesity before the age of 40 comparing to patients whose weight gain began after 40 years. Relatively early onset of arterial hypertension was discovered during the development of obesity at a young age. Men who developed obesity before the age of 40 years, had a higher number of metabolic syndrome components. Statistically significant increase in ALT and uric acid levels were revealed in men with newly diagnosed diabetes mellitus type 2, compared to those with previously diagnosed diabetes.

Conclusion

Clinical and biochemical particularities of the metabolic syndrome in men with different duration of obesity determine the need of advanced examination of individuals developing obesity before the age of 40 years for early diagnosis of associated conditions.

Key words

Metabolic syndrome, carbohydrate metabolism disorders, hyperuricemia

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Introduction

A lot of new data demonstrating controversial impact of metabolic abnormalities into metabolic syndrome (MS) development in men and women has been published during the last years. For example, Dallongeville J. et al. observed that body overweight, waist circumference, high density lipoprotein (HDL) levels have bigger impact on MS development in women, whereas in men systolic and diastolic blood pressure and apolipoprotein B levels are more important [1]. These data support the idea of different MS diagnostic criteria in men and women.

Epidemiological studies of the last years demonstrate a distinct interest to consequent manifestation of different MS syndromes in order to elaborate effective preventive strategy. According with several researchers, MS symptoms are characterized by distinct order of manifestation. For example, patients below 50 years often have abnormal carbohydrate metabolism and left ventricular myocardium remodeling, and patients above 50 years have dyslipidemia, abdominal obesity and arterial hypertension [2]. At the same time diabetes mellitus, 2 type (DM2) rarely occurs as the first manifestation of MS and is more common to develop after 50 years, when other components of MS have already appeared [3]. According with numerous studies, arterial hypertension (AH) is one of the dominating features of MS, and nowadays many researchers consider AH as part of MS [4].

Abdominal obesity (AO) is not always an early feature of MS, and the order of AH, carbohydrate metabolism disorders (CMD), and dyslipidemia manifestation can differ. According to population study made in Taiwan, abnormal lipid spectrum appears before the other MS components in both genders [5]. Another research group from Taiwan discovered gender differences in the sequence of MS manifestation: women start to have AO in adolescent age that develops into DM2 later, and young males initially demonstrate AO, increased levels of triglycerids (TG) and decreased levels of HDL, AH is added in middle age, and after all they develop DM2 [6]. Several studies demonstrated that MS components like AH, increased body weight, impaired glucose tolerance, and burdened family history may act as risk factors predisposing prediabetes change into evident DM [7].

The question of interrelation between ureic acid (UA) levels and DM are actively discussed in publications of the last years [8], and hyperuricemia is considered to be a DM2 predictor, increased UA concentration is present in the early stages of ICM and is related to micro- and macrovascular complications in the advanced stages of diabetes. Study made on Iranian population of patients with DM2 revealed direct correlation of MS components with UA levels [9]. The study of Rancho Bernardo[10] demonstrated that all causes of mortality are independently related to hyperuricemia, but mortality due to cardiovascular diseases (CVD) is connected with hyperuricemia just in people with impaired glucose tolerance. Epidemiological study of cardiovascular diseases and their risk factors in different regions of the Russian Federation (ESSE-RF) demonstrated independent association of all metabolic factors and hyperuricemia [11].

The knowledge of age, gender, clinical and biochemical features of metabolic syndrome, stages of its development and symptoms' manifestation would allow to perform effective preventive measures.

The aim of this study was to identify clinical and metabolic features of MS in males.

Materials and methods

299 men with MS aged 31-89 years underwent examination in the department of internal medicine of Ryazan Regional clinical hospital. All patients signed informed consent for participation in this study. This study was approved by local Ethic committee of Ryazan State Medical University. Inclusion criteria were the following: the presence of MS according with the criteria of Russian Society of Cardiology (2009) and signed informed consent.

Exclusion criteria were the following: DM1, severe kidney disorders (glomerular filtration rate (GFR)<30 mL/min quantified using CKD EPI), severe chronic heart failure, severe respiratory insufficiency, viral or alcohol liver lesions, autoimmune connective tissue disorders, congenital valve disease, mental disorders that could interfere with the contract between doctor and patient, patient's refusal of treatment.

Apart from history taking and standard physical examination patients underwent waist circumference (WC) and body mass index (BMI, quantified using Quetelet's formula). Laboratory tests included glucose detection using glucose oxidase method, oral glucose tolerance test, blood lipid spectrum (total cholesterol (TC), HDL, low density lipoproteins (LDL), TG) estimation was performed using enzymatic techniques and biochemical analyzer "Olympus AU-400" (Japan) that was also used for alanin aminotransferase (ALT) and aspartate aminotransferase (AST),

UA and creatinine detection. Transthoracic echocardiography (EchoCG) was done using ultrasound scanner Sequoia 512 (Siemens) in duplex mode, 2D mode, M-echo mode, tissue harmonic imaging and tissue doppler imaging. Abdominal ultrasonography was performed using LOGIQ Book XP (GE Medical Systems, China) ultrasound imaging system.

Statistical analysis of obtained data was done using Statistica 10.0 software. Data are present as median and 25-75 quartiles. Quantitative comparison of two independent groups was performed using Mann-Whitney U-test. Analysis of correlation between two variables was done using Spearman's rank correlation test (r). The level of significance (p) was taken as 0.05.

Results and discussion

The values of WC, the main component of MS, were 107.2 (100; 113) cm in men.

Patients were subdivided into the following age categories according to the WHO classification: aged 25-44 years referred to the young age, aged 44-60 years referred to the middle age, aged 60-75 years referred to the elderly age, aged 75-90 years referred to the very old age. Age distribution is present at the Figure 1.

Average BMI was 29.9±4.2 kg/m^2. BMI distribution of male patients with MS can be seen at the Figure 2.

52% of all patients had body overweight, and 9 men had AO combined with normal body weight.

Talking about additional MS diagnostic criteria, all patients had AH II-III degrees, and 87% of patients had it combined with coronary heart disease (CHD).

MS components representing abnormal lipid spectrum were the following: TG — 1.71 (1.23;2.47) mmol/L; HDL — 1.02 (0.89;1.22) mmol/L, LDL — 3.54 (2.8;4.39) mmol/L.

CMD that characterize one additional MS component were present in 41.7% and included: impaired fasting glycemia (IFG) — 33 patients (11%), impaired glucose tolerance (IGT) — 22 patients (7.3%), and DM2 — 70 patients (23.4%).

Age-related MS features in men (Figure 3) are characterized mostly by hypertriglyceridemia in young age (65.2%) with gradual decrease of its frequency in old age (17.4%). The frequency of CMD was

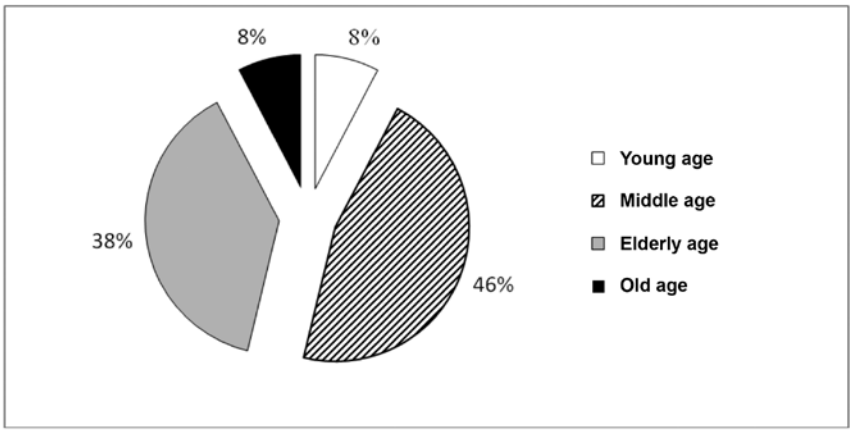

Figure 1. Age distribution of males

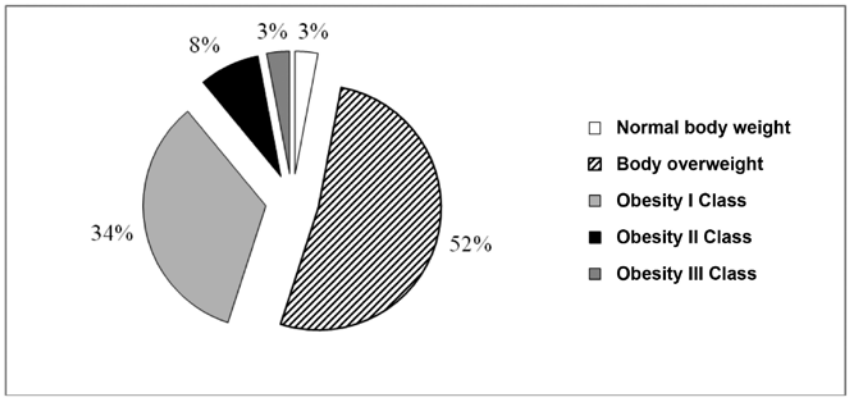

Figure 2. BMI distribution of males

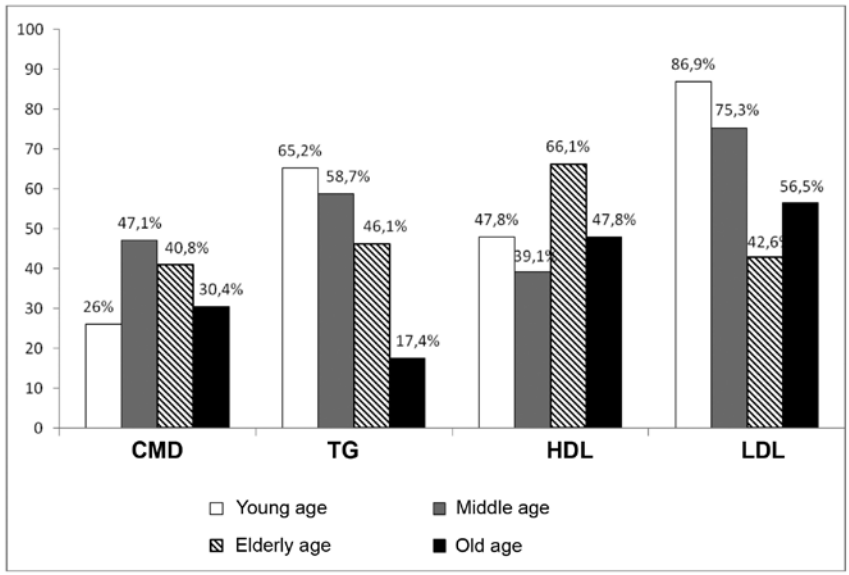

Figure 3. Age-related frequency of MS components in men

Table 1. **Comparison of patients in relation to the age of obesity onset**

Characteristic	Group 1 (n=168)	Group 2 (n=131	p
Age, years	49 (43.5; 54.5)	59 (57; 62)	0.000001
WC, cm	115.5 (105; 121)	112.5 (104; 117.5)	>0.05
MBI, kg/m^2	33 (31; 36.67)	31.4 (28; 33.7)	0.05
Duration of obesity, years	20 (10; 26.5)	8 (5; 15)	0.00002
Duration of AH, years	8 (5; 20)	8 (5; 20)	>0.05
Duration of DM2, years	2.5 (1; 6)	4 (4; 15)	>0.05
TC, mmol/L	5.9 (5.2; 7)	5.6 (4.6; 6.59)	>0.05
HDL, mmol/L	1 (0.87; 1.21)	1.13 (0.9; 1.33)	>0.05
LDL, mmol/L	4.1 (3.4; 4.9)	3.62 (2.8; 4.7)	>0.05
TG, mmol/L	1.88 (1.45; 1.56)	1.8 (1.25; 2.63)	>0.05

maximal in middle age (47.1%). HDL reduction is the most frequent in elderly man, and the occurrence of elevated LDL is maximal in young age (86.9%) and goes down in elderly age.

In men AO duration correlated directly with AH duration (r=0.3, p=0.025), with the sickness of interventricular septum (IVS, r=0.27, p=0.048) and had a reverse correlation with HDL levels (r=-0.34, p=0.011).

In order to study the features of MS development in men we subdivided them into the groups according with the age when the overweight started: Group 1 — 168 people reported to start body overweight before reaching 40 years, Group 2 — 131 patients reported the start of body weight after 40 years. Comparison of these two groups is present at Table 1.

The first group included significantly younger males with significantly higher BMI and obesity duration 2.5 times longer than in the second group. There were no statistically significant differences of WC between the groups. DM2 and burdened family history of DM2 was more frequent in the Group 1 (27.9% versus 17.5% and 40% versus 6.8%, respectively). Family history of obesity was more present in the Group 1 comparing with the Group 2 (32.2% versus 25.9%), whereas the family history of AH was found in the half of patients of both groups. More advanced obesity was combined with hepatomegaly: oblique vertical height of liver was 165.5 (153.5; 176) mm in the Group 1 versus 151 (144; 160) mm in the Group 2 (p=0.04), and other signs of non-alcoholic fatty liver disease were detected. According with the Table 1, there were no significant differences of lipid spectrum between groups.

Analyzing the number of MS components in two groups of men (Figure 4), we identified that increase of body weight in young age (Group 1) is combined with the higher number of MS components, even if the age of patients of the Group 2 was significantly higher.

According with the diagram (Figure 5), the most frequent combinations of MS components in the Group 1 include AO+AH+↑LDL (19.6%) and AO+AH+↓HDL+↑LDL+↑TG (17.8%), and the combination of AO+AH+↑LDL prevails also in the Group 2

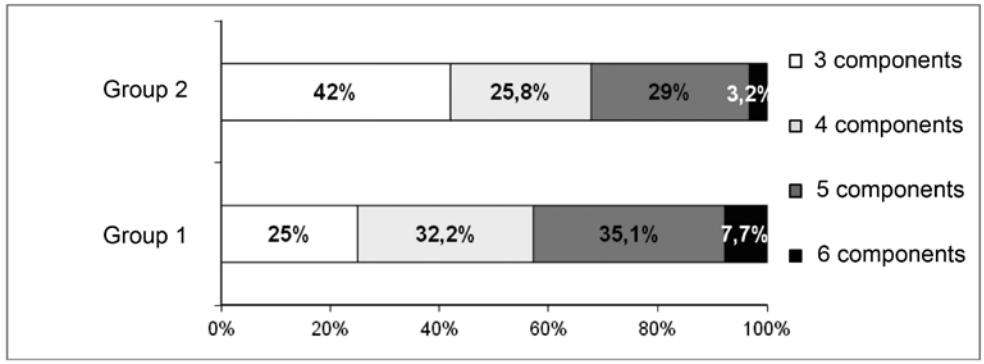

Figure 4. The frequency of different combinations of MS components

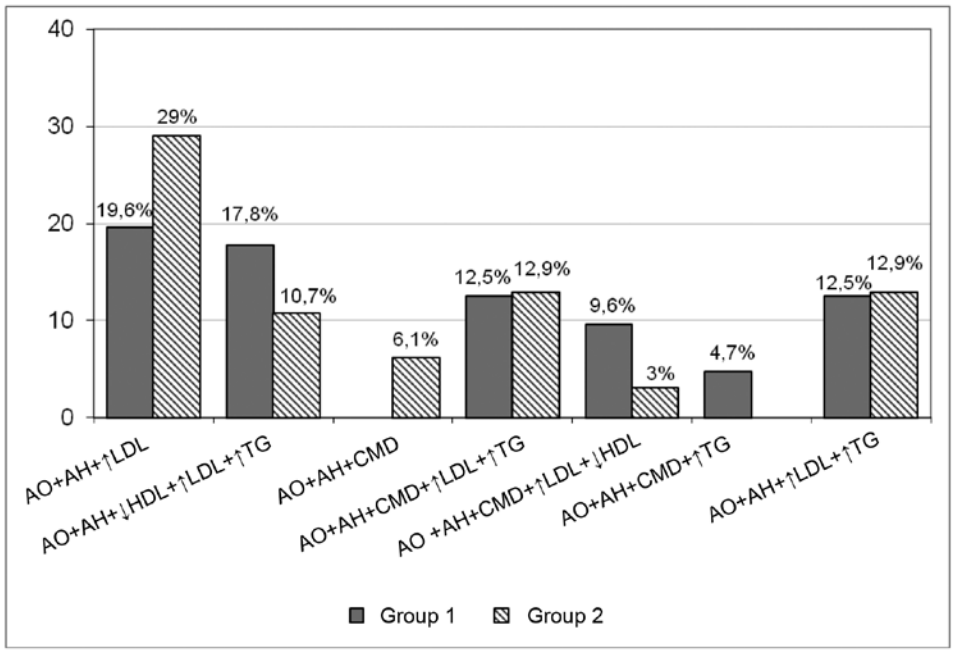

Figure 5. The frequency of various MS components in males (%)

(29%). The frequency of AO+AH+CMD+↑LDL+↑TG and AO+AH+CMD+↑TG combinations is equal in both groups. AO+AH+CMD is not present in the Group 1, and there is no AO+AH+CMD+↑ТГ combination in the Group 2. All combinations of MS components including ↑TG prevail with the same or higher frequency in the Group 1 that was proved with negative correlation between TG level and age of males (r=-0.33; p=0.000001).

We should notice that DM2 was firstly diagnosed in 25 men (35% of patients with DM2). According with this, we aimed to identify the differences with firstly and previously diagnosed DM2. We found out that patients with the onset of DM2 were younger and had shorter duration of obesity. We should not ignore the important biochemical features of firstly diagnosed DM2 in males like significantly higher levels of ALT and UA (Table 2).

Table 2. **Differences between male patients with different DM2 duration**

Characteristic	Firstly diagnosed DM2	Previously diagnosed DM2	p
Age, years	52 (50; 61)	60 (55; 69)	0.02
Obesity duration, years	4.75 (5; 9)	19 (15; 30)	0.03
ALT, U/L	36.5 (27; 46)	26 (18; 33)	0.005
UA, μM/L	451 (435; 461)	339 (308; 376)	0.023

Hyperuricemia was detected in 32.1% of males with MS (according to the ESSE-RF study, the same value in men aged 25-64 was 25.3% [11]). MS hyperuricemia was associated with TG levels (r=0.27, p=0.025). According to the results of several other studies, UA is related to TG levels, but independently from fasting insulin levels and obesity, thus demonstrating that the underlying mechanism is partially connected with insulin resistance and obesity [12].

In respect to elevated serum ALT levels in patients with firstly diagnosed diabetes, elevated ALT level was considered to be DM2 predictor in patients with AH [13] in one of available studies. Another one, published in 2016, demonstrated that border values of serum ALT and γ-GT (but not AST) levels were independent predictors of IFG and DM2 [14]. Several other studies have proved the connection between elevated serum ALT levels with DM2 risk [15, 16].

Conclusion

The analysis of clinical and biochemical features of MS in men allowed identifying of hypertriglyceridemia and elevated LDL levels in young age and maximal frequency of carbohydrate metabolism disorders in middle age patients. In 52% of cases MS was combined with body overweight in the studied group of male patients.

Men who manifested AO before the age of 40 (Group 1) had significantly higher BMI (but not WC) comparing with the patients who started to increase their body weight after reaching 40 years, and it demonstrates different fat tissue distribution in these groups. The same duration of AH in groups of men and significantly younger age of males of the Group 1 indicate earlier manifestation of AH in case of early development of obesity. Although the patients of the Group 1 were significantly younger, development of obesity before the age of 40 was characterized with higher number of MS components.

Men with firstly diagnosed DM2 had statistically significant increased ALT and UA serum levels comparing with the people with previously diagnosed DM. Our results go along with the results of several other studies and prove the role of these biochemical markers in early diagnostics of impaired carbohydrate metabolism.

Conflict of interest: None declared.

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