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RELATIONSHIP BETWEEN METABOLIC SYNDROME COMPONENTS IN PATIENTS WITH RESISTANT ARTERIAL HYPERTENSION

I. P. Shmakova, S. A. Panina, P. A. Shishova

Odessa National Medical University of the Ministry of Health of Ukraine

Abstract

Metabolic syndrome (MS) is a complex of interrelated pathological conditions based on insulin resistance, obesity, dyslipoproteinemia, arterial hypertension (AH). MS is a predictor of the cardiovascular disease, type 2 diabetes mellitus (DM), cancer and premature death. The incidence of type 2 diabetes increases with age and is 25.2% among the elderly. The prevalence of prediabetes or metabolic syndrome was approximately three times higher. Heart failure is another important cause of morbidity and mortality from the cardiovascular disease. Recent studies have shown that the incidence of hospitalizations for heart failure (adjusted for age and gender) was twice as high in patients with diabetes compared with patients without diabetes. Patients with hypertension and abdominal obesity (AO) have an increased risk of various complications: type 2 diabetes -5-9 times, stroke - 7 times, coronary heart disease - 4 times and mortality - 2 times. Objective: To analyze the relationship between the components of the metabolic syndrome in patients with resistant arterial hypertension (RAH). Materials and methods. A retrospective analysis of case histories of 120 patients, including 52 men (43.33%) and 68 women (56.67%) with a diagnosis of RAH and signs of MS. The presence of concomitant pathology, the level of office arterial pressure, pulse pressure (PP) were calculated; body weight, height with calculation of body mass index (BMI); waist circumference (WC), the levels of low-density lipoprotein (LDL) and high-

density lipoprotein (HDL), triglycerides (TG), and plasma glucose were studied. Student's criterion was used to assess the degree of significance of the differences, $p \leq 0.05$ was taken as the critical level of significance. Pearson's correlation coefficient was used. Disorders of carbohydrate metabolism among patients with MS and RAH is 67.50%, of which type 2 diabetes makes 50.83%, impaired glucose tolerance - 16.67%. Patients with impaired carbohydrate metabolism are 2 times more likely to have complications of hypertension and lower HDL. Women with MS and RAH were significantly older than men and more often had concomitant pathology: morbid obesity ($p < 0.05$), type 2 diabetes mellitus ($p < 0.05$), chronic cerebral ischemia ($p < 0.05$), higher body mass index ($p < 0.01$). Strong correlation between WC and BMI ($r = 0.707$; $p<0.001$), weak direct correlations between WC and PP ($r = 0.231$; $p<0.05$) and WC and TG ($r = 0.221$; $p<0.05$), weak feedback between WC and age ($r = -0.188$; $p<0.05$), and for men direct correlations between WC and TG were confirmed ($r = 0.454$; $p<0.001$), BMI and TG ($r = 0.454$, $p<0.002$).

Key words: Metabolic syndrome; resistant arterial hypertension; interconnection.

Background. Metabolic syndrome (MS) is a complex of interrelated pathological conditions based on insulin resistance, obesity, dyslipoproteinemia, arterial hypertension (AH). MS is a predictor of the cardiovascular disease, type 2 diabetes mellitus (DM), cancer and premature death [1]. According to 2017 data, about 30.2 million adults aged 18 and older suffered from type 2 diabetes in the United States. The incidence of type 2 diabetes increases with age and is 25.2% among the elderly. The prevalence of prediabetes or metabolic syndrome was approximately three times higher. According to a global study of obesity in 195 countries, conducted in 2015, 604 million adults and 108 million children were obese [2]. Coronary heart disease (CHD), cerebrovascular disease or peripheral artery disease of atherosclerotic origin are the leading cause of morbidity and mortality among people with diabetes. Heart failure is another important cause of morbidity and mortality from the cardiovascular disease. Recent studies have shown that the incidence of hospitalizations for heart failure (adjusted for age and gender) was twice as high in patients with diabetes compared with patients without diabetes [3]. However, according to the literature, patients with hypertension and abdominal obesity have an increased risk of various complications: type 2 diabetes -5-9 times, stroke - 7 times, coronary heart disease - 4 times and mortality - 2 times [8, 9].

Objective: To analyze the relationship between the components of the metabolic syndrome in patients with resistant arterial hypertension (RAH).

Materials and methods. A retrospective analysis of case histories of 120 patients, including 52 men (43.33%) and 68 women (56.67%) with a diagnosis of RAH and signs of MS. The average age of patients was (66.71 ± 11.05) years. The diagnosis of MS was established on the basis of criteria recommended by the International Association for the Study of Diabetes (IDF, 2005) [1, 2]. The diagnosis of RAH was made in the absence of achieving the target level of arterial pressure (AP) on the background of taking three antihypertensive drugs (AHD) in maximum doses, one of which was a diuretic [4]. The presence of concomitant pathology, the level of office arterial pressure, pulse pressure (PP) were calculated; body weight, height with calculation of body mass index (BMI); waist circumference (WC), the levels of low-density lipoprotein (LDL) and high-density lipoprotein (HDL), triglycerides (TG), and plasma glucose were studied. Student's criterion was used to assess the degree of significance of the differences, $p \leq 0.05$ was taken as the critical level of significance. Data in all tables are presented as mean + - standard deviation. Pearson's correlation coefficient was used.

Results and discussion. Among the examined 2 (1.67%) had the stage 1 hypertension, 66 (55.00%) - stage 2 and 52 patients (43.33%) - stage 3. Impaired glucose tolerance (IGT) was found in 20 (16.67%), type 2 diabetes - in 61 (50.83%) patients. The clinical characteristics of the patients depending on the state of carbohydrate metabolism (CM) (group I - 39 patients without CM disorders, group II - 81 patients with CM disorders) are shown in Table 1.

Table 1 - **Clinical characteristics of patients with metabolic syndrome depending on the state of carbohydrate metabolism**

Indices	I group, n=39	II group, n=81
Age, years	64.97±12,72	67.54±10.84
BMI, kg/m^2	34.09±4.99	34.29±6.64
Waist circumference, cm	108.33±12,38	109.04±15.40
SAP, mm Hg	156.62±10.15	153.98±9.21
DAP, mm Hg	91.82±7.41	90.37±7.12
Pulse pressure, mm Hg	64.79±7.39	63.60±7.65
Blood glucose, mmol/l	5,38±0,84	9.10±3.35
TG, mmol/l	1.59±0.75	1.85±1.16
HDL, mmol/l	1.23±0.29	1.08±0.30
LDL, mmol/l	3.48±1.06	3.29±1.19*
Average amount of AHD per a patient	3.56±0.82	3.58±0.76

Note: p is the significance of the differences between groups * - $p < 0.05$

It was found that 51.85% of patients with CM disorders had AH of stage 3, and in the absence of 25.64% (p <0.01). BMI, WC and the ratio of degrees of obesity in the groups did not differ. In the group II the level of antiatherogenic fraction of HDL was lower by 12.2% than in the group I.

Table 2 shows the clinical characteristics of patients with MS and RAH depending on gender.

Table 2 - **Clinical characteristics of patients with metabolic syndrome depending on the gender**

Indices	Men, n= 52	Women, n= 68
Mean age, years	63.69±12.30	69.01±10.35*
1st stage of HD, %	1.92	1.47
2nd stage of HD, %	51.92	57.35
3rd stage of HD, %	46.15	41.18
IGT, %	25.00	10.29*
DM, %	40.38	58.82*
CCI (Chronic cerebral ischemia), %	67.31	85.29*
BMI, kg/m^2	32.69±6.5	35.28±5.8**
Overweight, %	30.77	17.65
Obesity of the 1st degree, %	50.00	36.76
Obesity of the 2nd and 3rd degree, %	19.23	45.59**
Waist circumference, см	110.52±12.43	107.50±15.77
SAP, mm Hg	155.94±10.42	153.99±8.84
DAP, mm Hg	91.60±7.45	90.26±7.03
Pulse pressure, mm Hg	64.35±7.14	63.72±7.84
Blood glucose, mmol/l	7.78±3.11	8.01±3.44
TG, mmol/l	1.69±0.79	1.82±1.21
HDL, mmol/l	1.10±0.30	1.16±0.31
LDL, mmol/l	3.28±1.02	3.41±1.24
Average amount of AHD per a patient	3.54±0.90	3.60±0.67

Note: p is the significance of the differences between men and women.

* - p <0.05; ** - p <0.01.

The data given in tables 1, 2 show that women more often (82.35%) than men (69.23%) suffered from morbid obesity (BMI > 35 kg / m^2) which along with age, is a risk factor for many diseases, in particular, type 2 diabetes and chronic cerebral ischemia (CCI), which was observed in our patients. However, the frequency of RAH of the stage 3, mean arterial pressure, PP and laboratory indices did not differ significantly from men. IGT was more common in men than in women (p<0.05).

The presence of overweight and obesity is one of the reasons for the formation of hypertension, it increases cardiovascular risk and the risk of total mortality [4,5]. Obesity impairs arterial pressure control and increases the incidence of RAH (50% of overweight patients do not reach the target arterial pressure) [6]. To assess the impact of obesity on the course of hypertension, the presence of concomitant pathology, laboratory indices, all patients were divided into groups depending on BMI.

Table 3 - **Clinical characteristics of the patients with metabolic syndrome depending on body mass index**

Indices	BMI<35kg/m^2, n=79	BMI≥35 kg/m^2, n=41
Women, %	46.83	75.61**
Age, years	67.13±12.11	65.90±10.31
1st stage of HD, %	2.53	0
2nd stage of HD, %	56.96	51.22
3rd stage of HD, %	40.51	48.78
IGT, %	20.25	9.76
DM, %	48.10	56.10
CCI, %	72.15	87.80*
BMI, kg/m^2	30.78±2.65	40.86±5.45**
Waist circumference, см	102.73±9.93	120.51±14.64**
SAP, mm Hg	154.39±9.52	155.68±9.71
DAP, mm Hg	90.95±7.66	90.63±6.36
Pulse pressure, mm Hg	63.44±7.58	65.05±7.49
Blood glucose, mmol/l	7.90±3.18	7.93±3.55
TG, mmol/l	1.62±0.88	2.06±1.29
HDL, mmol/l	1.13±0.29	1.15±0.34
LDL, mmol/l	3.30±1.10	3.47±1.25
Average amount of AHD per a patient	3.51±0.71	3.71±0.87

Note: p is the significance of differences between groups.

* - p <0.05; ** - p <0.01.

According to Table 3, the incidence of morbid obesity among patients with MS and RAH was 2 times higher, of which 75.61% were women. Morbid obesity was combined with abdominal obesity: WC of the patients with BMI ≥35 kg / m^2 was 17.3% higher than that of the patients with BMI <35 kg / m^2. CCI in the group of morbid obesity occurred 15% more frequently (p<0.05).

Tables 4 and 5 show the clinical characteristics of men and women depending on WC.

According to the criteria of IDF 2005, abdominal obesity in men is determined at WC >94 cm for Europeans, and by more "soft" criteria of Adult Treatment Panel (ATR III, 2001) at WC>102 cm [1, 2]. Among the men surveyed, only 11 had normal WC according to ATR

III criteria (group I), but these patients were significantly older, had a lower BMI and morbid obesity, lower PP and TG levels than the patients with severe abdominal obesity (WC>120 cm). Thus, the patients with borderline AO values (94-100 cm) have fewer metabolic risk factors but they remain in a high cardiovascular risk zone.

Table 4 - **Clinical and laboratory characteristics of the men with metabolic syndrome depending on the waist circumference**

Indices	WC<100 cm, n=11 (1)	WC 100-119 cm, n=29 (2)	WC ≥ 120 cm, n=12 (3)	P		
Age, years	72.00±8.22	62.90±12.81	58.00±10.76	1-2*	1-3 **	
DM+IGT, %	63.64	65.52	66.67			
DM, %	45.45	34.48	50.00			
BMI, kg/m^2	29.10±2.45	31.51±2.87	38.05±4.74	1-2 *	1-3 ***	2-3 ***
Overweight, %	63.64	31.03	0		1-3 ***	2-3 ***
Obesity of the 1st degree, %	36.36	62.07	33.33			
Obesity of the 2nd degree, %	0	3.45	33.33		2-3 *	1-3 *
Obesity of the 3rd degree, %	0	3.45	33.33		1-3 **	2-3 **
Waist circumference, cm	95.55±2.16	108.69±5.53	128.67±6.44	1-2 ***	1-3 ***	2-3 ***
SAP, mm Hg	155.00±10.72	154.24±8.85	160.92±12.81			
DAP, mm Hg	93.82±8.96	89.90±6.45	93.67±7.83		1-3*	
Pulse pressure, mm Hg	61.18±7.03	64.34±7.37	67.25±6.36		1-3*	
TG, mmol/l	1.39±0.72	1.55±0.74	2.32±0.68		1-3 **	2-3 **
LDL, mmol/l	2.92±0.95	3.28±0.96	3.60±1.18			
Average amount of AHD per a patient	3.45±0.69	3.48±0.74	3.75±1.36			

Note: p_{1-2} is the difference between groups I and II, p_{1-3} is the difference between groups I and III, p_{2-3} is the difference between groups II and III.

* - p <0.05; ** - p <0.01, *** - p <0.001.

Being overweight and obese have been linked to insulin resistance and MS. However, AO is more correlated with MS than elevated BMI [7].

Table 5 - **Clinical and laboratory characteristics of the women with metabolic syndrome depending on the waist circumference**

Indices	WC<100 cm, n=19 (1)	WC 100-119 cm, n=35 (2)	WC ≥ 120 cm, n=14 (3)	P		
Age, years	70.79±11.76	69.37±9.84	65.71±9.55			
DM+IGT, %	78.95	62.86	71.43			
DM, %	57.89	57.14	64.29			
BMI, kg/m^2	29.41±2.87	35.23±3.90	44.61±6.82	1-2 ***	1-3 ***	2-3 ***
Overweight, %	57.89	2.86	0	1-2 ***	1-3 ***	
Obesity of the 1st degree, %	36.84	48.57	7.14		1-3 *	2-3 ***
Obesity of the 2nd degree, %	5.26	37.14	21.43	1-2 **		
Obesity of the 3rd degree, %	0	11.43	71.43	1-2 *	1-3 ***	2-3 ***
Waist circumference, cm	90.63±3.30	107.20±5.41	131.14±13.08	1-2 ***	1-3 ***	2-3 ***
SAP, mm Hg	153.79±9.21	152.89±7.89	157.00±10.4			
DAP, mm Hg	91.26±7.29	89.77±7.27	90.14±6.41		1-3 *	
Pulse pressure, mm Hg	62.53±8.23	63.11±6.49	66.86±9.94			
TG, mmol/l	1.57±0.83	1.92±1.24	1.94±1.59		1-3 **	2-3 **
LDL, mmol/l	2.92±1.27	3.73±1.24	3.24±1.02			
Average amount of AHD per a patient	3.47±0.61	3.57±0.61	3.86±0.86			

Note: p_{1-2} is the difference between groups I and II, p_{1-3} is the difference between groups I and III, p_{2-3} is the difference between groups II and III.

* - p <0.05; ** - p <0.01, *** - p <0.001.

Unlike men, there was no age difference between the groups. All patients had AO (WC>80 cm) according to IDF criteria 2005. Compared with men WC in women of group 1 was lower, and 2 and 3 groups - did not differ, which indicates the spread of increasing AO in

parallel with an increase in BMI women. There is no significant difference between the frequency of carbohydrate and lipid profile disorders in men and women.

The DECODE study found that a slight increase in blood pressure and impaired glucose tolerance increase the risk of cardiovascular disease in postmenopausal women. There is a hypothesis of gender differences in the pathogenesis of MS, in men the leading predictor of MS is AO regardless of age, in women the main triggers for the formation of MS - diabetes and menopause [7].

Correlation coefficients were calculated for different indicators (Table 6).

Table 6 - **Correlations between some components of the metabolic syndrome**

Interrelation between:	r	r_1	r_2	r^2	t	P
WC and age	-0.188	-0.010	-0.356	0.036	2.08	<0.05
- only men	-0.221	0.055	-0.466	0.049	1.60	>0.05
- only women	-0.140	0.102	-0.366	0.019	1.15	>0.05
WC and TG	0.221	0.385	0.043	0.049	2.41	<0.05
- only men	0.454	0.647	0.207	0.207	3.54	<0.001
- only women	0.143	0.369	-0.099	0.020	1.15	>0.05
WC and PP	0.231	0.394	0.054	0.053	2.58	<0.05
- only men	0.235	0.477	-0.041	0.055	1.71	>0.05
- only women	0.226	0.441	-0.013	0.051	1.88	>0.05
WC and BMI	0.707	0.787	0.604	0.500	10.86	<0.001
- only men	0.768	0.861	0.627	0.590	8.49	<0.001
- only women	0.759	0.845	0.636	0.577	9.48	<0.001
BMI and PP	0.091	0.265	-0.090	0.008	0.99	>0.05
- only men	0.050	0.319	-0.226	0.003	0.41	>0.05
- only women	0.131	0.358	-0.111	0.017	1.07	>0.05
BMI and TG	0.179	0.347	0.000	0.032	1.93	>0.05
- only men	0.439*	0.636	0.189	0.193	3.39	<0.002
- only women	0.082*	0.315	-0.159	0.007	0.66	>0.05

r is the Pearson correlation coefficient; r_1 and r_2 - 95% confidence interval for the correlation coefficient - upper and lower limits, respectively; r^2 - coefficient of determination; t is the Student's t test.

* the difference between the correlation coefficients is significant, p <0,05.

For all patients, a strong correlation was found between WC and BMI ($r = 0.707$; $p<0.001$), the correlation coefficients in women and men did not differ ($p = 0.91$). There is a weak direct correlation between WC and PP ($r = 0.231$; $p<0.05$), but it is absent between PP and BMI. Thus, it is abdominal rather than peripheral obesity that is associated with PP as one of the cardiovascular risk factors. A weak inverse correlation was found between WC and age ($r = -0.188$; $p<0.05$).

For all patients there was a weak direct correlation between WC and TG ($r = 0.221$; $p<0.05$), it was confirmed for men (direct, moderate ($r = 0.454$; $p<0.001$)), but not for women. For men, a direct moderate association between BMI and TG was also confirmed ($r = 0.439$; $p<0.002$).

Conclusions:

1. Disorders of carbohydrate metabolism among patients with MS and RAH is 67.50%, of which type 2 diabetes makes 50.83%, impaired glucose tolerance - 16.67%.

2. Patients with impaired carbohydrate metabolism are 2 times more likely to have complications of hypertension and lower HDL.

3. Women with MS and RAH were significantly older than men and more often had concomitant pathology: morbid obesity ($p <0.05$), type 2 diabetes mellitus ($p <0.05$), chronic cerebral ischemia ($p <0.05$), higher body mass index ($p <0.01$).

4. Strong correlation between WC and BMI ($r = 0.707$; $p<0.001$), weak direct correlations between WC and PP ($r = 0.231$; $p<0.05$) and WC and TG ($r = 0.221$; $p<0.05$), weak feedback between WC and age ($r = -0.188$; $p<0.05$), and for men direct correlations between WC and TG were confirmed ($r = 0.454$; $p<0.001$), BMI and TG ($r = 0.454$, $p<0.002$).

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