CHARACTERISTICS OF CLINICAL AND METABOLIC MANIFESTATIONS OF OBESITY IN PATIENTS WITH ARTERIAL HYPERTENSION AND CHRONIC KIDNEY DISEASE

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Abstract*. 113 patients with hypertension were selected according to the inclusion criteria (hypertension stage I–II, degree 1–3, absence of kidney pathology). Body mass index does not determine the obesity phenotype. In patients with complicated obesity, the proportion of fat mass is higher than in metabolically healthy obesity and is associated with increased levels of glucose, leptin, and the degree of insulin resistance. A decrease in the proportion of active cell mass is associated with an increase in adipocytokines.*
Keywords*: chronic kidney disease, degree of obesity, arterial hypertension.*

The high prevalence of obesity represents a serious medical and social problem. Research in recent years has proven that the risks of developing cardiovascular diseases (CVD) are associated not so much with the volume of fat mass, but with its hormonal and metabolic activity, which served as the basis for the formation of the concept of metabolic health, which formed the basis of the modern classification of obesity [2, 4 , 8, 11].

Obesity is also one of the significant risk factors for the development of chronic kidney disease (CKD), while at the same time there is no consensus on the contribution of different obesity phenotypes to the development of renal disorders. Pilot studies have proven the possibility of using markers of early renal damage to identify renal dysfunction in patients with CVD and diabetes mellitus. There is limited data on the relationship between markers of preclinical kidney damage and parameters characterizing the hormonal-metabolic component of obesity. According to published data, the development of chronic subclinical inflammation in obese patients contributes to the progression of metabolic disorders and the formation of arterial hypertension (AH) [4, 5].

Metabolic disorders are widespread among the adult population, and metabolic syndrome (MS) as a combination of hypertension with dyslipidemia and impaired glucose tolerance (IGT) reaches a frequency of 25-35% in the general population [1, 3, 5, 6]. Mortality from cardiovascular diseases among people with MS was 6 times higher than among people without these disorders, and the most significant predictors of mortality include microalbuminuria (MAU).

Goal of the work. To study the clinical and metabolic manifestations of chronic kidney disease against the background of arterial hypertension in different obesity phenotypes.

Materials and methods. We selected 113 patients with hypertension stages I–II, degrees 1–3 (provided there was no renal pathology, i.e., a history of kidney disease, structural lesions of the parenchyma and vessels of the kidneys during ultrasound examination, changes in urinary sediment and urine density, proteinuria , decrease in GFR less than 60 ml/min/1.73 m²) at the age of 40-55 years (average age - 46.34±4.6 years). All study patients were divided into 3 study groups:

Group 1: patients with hypertension without obesity (BMI less than 30 kg/m²) (n = 41);

Group 2: patients with hypertension and obesity (BMI ≥ 30 kg/m²), but without metabolic changes (i.e., without IGT, hyperglycemia, DLP, GTG) – (n = 37);

Group 3 – metabolically complicated obesity, in which, in addition to obesity (BMI ≥30 kg/m²) and hypertension, impaired glucose tolerance (IGT) and dyslipidemia were noted (n = 45).

Inclusion criteria and methods for assessing MS included: blood pressure (BP) level of patients with hypertension: systolic (SBP) - 140-180 mm Hg. Art., diastolic (DBP) - 90-110 mm Hg. Art., lipid levels in the blood serum: total cholesterol (TC) ≥5.4 mmol/l, triglycerides (TG) ≥ 1.7 mmol/l, low-density lipoproteins (LDL) ≥3 mmol/l, atherogenic coefficient (AC) ≥ 3.5. Abdominal type of obesity - ratio of waist circumference (WC) to hip circumference (HC) - WC/HC ≥0.80; body mass index (BMI) ≥ 30 kg/m2, the degree of insulin resistance was calculated using the HOMA-IR index. The metabolic activity of adipose tissue was assessed by the level of leptin, adiponectin, and resistin. To assess the functional state of the kidneys, we examined the level of serum creatinine (CC), calculation of glomerular filtration rate (GFR), proteinuria more than 30 mg/day (albuminuria -AU). A metabolically healthy obesity phenotype was defined as the presence of obesity without hypertension, dyslipidemia (DLP), hypertriglyceridemia (HTG), hyperglycemia and/or IGT.

Exclusion criteria: endocrine forms of obesity, secondary hypertension, stage III hypertension, diabetes, autoimmune diseases, bronchial asthma, cancer, pathology of the nervous system, mental disorders associated with CVD (severe coronary artery disease, acute coronary syndrome, unstable angina, chronic heart failure (CHF), high grade cardiac arrhythmias), occlusive peripheral arterial disease, severe liver dysfunction (more than twofold increase in transaminases), pregnancy, lactation, allergic reactions to taking antihypertensive drugs, refusal of the study.

The research results were processed using parametric and nonparametric statistics using the Microsoft Excel statistical software package.

Research results and discussion

The general characteristics of the patients and the distribution of cardiometabolic risk factors are presented in Table 1. According to WHO criteria, all patients had a moderate degree of increase in blood pressure, where SBP averaged 134.8 ± 15.4 mm Hg for group I. Art. and DBP - 91.4±7.32 mmHg. Art., in the second group - 158.3±2.41 and 99.3±5.4 mmHg. Art. ($p<0.01$) and in the 3rd group – 166.1±16.1 per 103.1±6.8 mm Hg, respectively. ($p<0.005$). BMI in the 1st, 2nd and 3rd groups, respectively, was 25.4±2.62, 28.4±2.73($p<0.01$) and 32.8±4.81($p<0.01$) kg/m2.

Table 1.

General characteristics of patients and distribution of cardiometabolic risk factors

Index	1- group (n=41)	2- group (n=37)	3- group (n=45)
Age, years	41,7 ±4,5	45,3±5,1	49,8±7,4**∞
Men, abs (%)	26 (63,4%)	19 (51,4%)	21 (46,7%)
Women, abs (%)	15 (36,6%)	18 (48,6%)	24 (53,3%)
Body mass index, kg/m^2	25,4±2,62	28,4±2,73**	32,8±4,81***∞

SBP, mmHg Art.	134,8±15,4	158,3±12,9**	166,1±16,1***
DBP, mmHg Art.	91,4±7,5	99,3±5,4**	103,1±6,8***
Duration of hypertension, year	4,45±2,22	6,24±2,39*	7,48±2,31***
1st degree of hypertension, abs (%)	19 (46,3%)	9 (24,3%)	5 (11,1%)
2nd degree hypertension, abs (%)	15 (36,6%)	17 (45,9%)	18 (40,0%)
3 degree hypertension, abs (%)	7 (17,1%)	11 (29,7%)	22 (48,9%)
Stage I headache, abs (%)	25 (61%)	19 (51,4%)	15 (33,3%)
Stage II headache, abs (%)	16 (39%)	18 (48,6%)	30 (66,7%)
Family history of hypertension, abs (%)	22 (53,6%)	25 (61,1%)	36 (80,0%)
Tobacco smoking, abs (%)	15 (36,6%)	16 (38,9%)	23 (51,1%)

Note: **(p<0.01), ***(p<0.005) in relation to the data of the 1st group;
∞ (p<0.05) between the 2nd and 3rd study groups.

During the study, patients with stage II hypertension (HD) were identified - 16 (39%) patients of the 1st group, 18 (48.6%) patients of the 2nd group with hypertension and obesity without metabolic changes and 30 (66.7% of patients with hypertension with metabolically complicated obesity (IMG≥30 kg/m2 +GTG, DLP, IR).The duration of hypertension in patients of the 1st group was 4.45±2.22, in the 2nd group 6.24±2.39 (p<0.01) and in patients of group 3 7.48±2.31 years (p<0.005).

Table 2.

Metabolic profile indicators among patients in the study groups

Index	1- group (n=41)	2- group (n=37)	3- group (n=45)
Blood glucose, mmol/l	4,96±0,41	5,13±0,36	5,84±0,62**
IR, HOMA-IR	1,74±0,64	2,47±0,76**	4,59±1,13***∞
OBHss, mmol/l	4,45±0,46	5,16±0,63**	6,74±1,21***∞
LDL cholesterol, mmol/l	2,25±0,44	2,76±0,75	3,82±1,18***∞
HDL cholesterol, mmol/l	2,32±0,65	1,98±0,55*	1,54±0,53**
TG, mmol/l	0,87±0,33	0,99±0,26	1,76±0,52***∞
Leptin, ng/ml	7,94±4,52	13,73±5,28***	21,82±9,41*** ∞
Adiponectin, мкg/ml	29,12±2,2	18,54±2,4***	6,49±2,92***∞
Resistin, , ng/ml	8,81±2,37	21,67±4,71***	35,79±5,24*** ∞

Note: *(p<0.05), ***(p<0.005) in relation to the data of the 1st group;

∞ ($p<0.05$) between the 2nd and 3rd study groups.

Based on the principles of group distribution depending on the presence of obesity and metabolic changes, patients of the 2nd and 3rd groups also differed in metabolic profile indicators. Thus, in patients of the 2nd and 3rd groups with obesity, significant changes in metabolic profile parameters were observed, in contrast to patients in the 1st group with hypertension without obesity. Along with the high indicators of the lipid profile of patients with hypertension and obesity of the 2nd ($p<0.01$) and 3rd group ($p<0.005$) compared with the 1st group of the study, there was also an increase in the IR indicator by 42% ($p<0.01$) and 69% ($p<0.005$) in the 2nd and 3rd study groups, respectively.

The study of the metabolic activity of adipose tissue also showed significant differences in the levels of leptin, adiponectin and resistin in the blood. Patients of the 2nd and 3rd study groups differed statistically significantly from the data of the 1st study group in leptin parameters by 1.76 ($p<0.01$) and 2.72 ($p<0.005$) times. The value of adiponectin in the 2nd and 3rd groups with hypertension and obesity was 46.3% ($p<0.01$) and 4.5 times ($p<0.005$), respectively, in contrast to the data in the 1st group. Significant changes in the parameters of metabolic activity of adipose tissue were confirmed by significant changes in the blood resistin index of 2.5 ($p<0.005$) and 4.1 ($p<0.005$) times compared with the data of the 1st group with hypertension without obesity.

Patients of the 2nd and 3rd groups with hypertension and obesity, depending on the presence of metabolic manifestations, also statistically significantly differed according to the parameters of metabolic activity of adipose tissue ($p<0.05$) (Table 2.)

Table 3. Functional state of the kidneys in the study groups.

Index	1- group (n=41)	2- group (n=37)	3- group (n=45)
CC, mmol/l	82,3±10,24	97,15±11,91*	118,26±16,73**∞
GFR ml/min/m2	106,84±18,64	88,27±15,44	106,61±11,26
GFR ml/min/m2	22,56±11,11	36,72±19,41	87,12±39,85
Number of patients without AS, abs (%)	27 (65,9%)	11 (29,7%)	4 (8,9%)
Number of patients with AU≤30 g/l, abs (%)	9(21,9%)	17 (45,9%)	15 (33,3%)
Number of patients with AU 30-300 g/l, abs (%)	5 (12,2%)	9 (24,3%)	17 (37,8%)
Number of patients with AU >300g/l, abs (%)	-	-	9(20,0%)

Note: **($p<0.01$), ***($p<0.005$) in relation to the data of the 1st group;
∞ ($p<0.05$) between the 2nd and 3rd study groups.

Elevated levels of serum creatinine were significantly more common in obese hypertensive patients. Daily albumin excretion was also higher in patients of the second group, but was significant only in patients with hypertension in combination with metabolically complicated obesity ($p<0.005$).

The highest level of AU was also observed in patients with hypertension with obesity and IR (87.12±39.85 g/l) and was detected in 20% (AU >300g/l) and 17 (37.8% - with AU 30-300g). /l) versus 5 (12.2%) patients with hypertension without obesity. In general, patients with hypertension in combination with metabolic disorders more often develop cardiorenal syndrome

with moderate impairment of nitrogen excretory function of the kidneys, and microalbuminuria is detected. High blood pressure levels and the development of IR, DLP and HTG lead to a deterioration in the functional state of the kidneys. Albuminuria, a decrease in glomerular filtration rate, and an increase in creatinine levels become the main manifestations of cardiorenal syndrome in patients with hypertension in combination with obesity, where IR is a precursor of these disorders and the cause of the development and progression of kidney damage.

Based on scientific data and the results of the study, a concept for the development of obesity phenotypes and the formation of the cardiorenal continuum was formed. The interrelationship of metabolic, hormonal and genetic factors determines the phenotypic variants of obesity: metabolically healthy obesity with preserved insulin sensitivity, metabolically healthy obesity with insulin and leptin resistance, metabolically complicated obesity and metabolic changes without obesity. The results of the study allow us to conclude that in obese patients in the absence of clinical signs of CKD and with optimal GFR and albuminuria, signs of renal dysfunction were identified.

Thus, we can conclude that significant relationships were identified between a decrease in GFR and an increase in hormonal and metabolic parameters in groups 2 and 3. It should be noted that in group 3 with hypertension and metabolically complicated obesity, an increase in GFR was associated with an increase in leptin and adiponectin values.

Conclusions:

1. In patients with complicated obesity, the proportion of fat mass is higher than in metabolically healthy obesity and is associated with increased levels of glucose, leptin, and the degree of insulin resistance. A decrease in the proportion of active cell mass is associated with an increase in adipocytokines. Patients with complicated obesity as metabolic and hormonal disorders progress.

2. In patients with metabolically healthy obesity, the dynamics of an increase in adipose tissue volume and leptin levels determine the formation of renal hyperfiltration. An early marker of glomerular and tubular dysfunction in the absence of albuminuria in patients with increased levels of insulin resistance are GFR and AU values.

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