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The Study of Gender Characteristics of Arterial Hypertension in the First and Second Stages

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Abstract

To clarify gender differences in the status of patients suffering from stage 1 and 2 arterial hypertension, 80 patients of the second mature age suffering from arterial hypertension were examined. They were divided into 2 groups. The first included 44 patients with stage 1 arterial hypertension, and the second group included 36 patients with stage 2 of the disease. In both sexes, in the case of stage 1 arterial hypertension, the level of arterial pressure corresponds to stage 1. At stage 2, blood pressure values in men are at the level of 1 degree, and in women, they correspond to 2 degrees. The amounts of total cholesterol and cholesterol in the composition of low-density lipoproteins were above the normative level and prevailed in women of both groups. At the 1st stage of hypertension in women, there was a more pronounced imbalance in the amounts of thromboxane B_2 and 6-keto-prostaglandin $F_{1\alpha}$, which was aggravated during the growth of the pathology stage. In men, glomerular filtration was preserved in both groups. From the very beginning of the disease in women, it was reduced, gradually worsening with the progression of the disease. The thickness of the vascular intima and copper in women already at stage 1 was higher than in men and increased with the severity of the pathology. It can be thought that in women, already during the formation of arterial hypertension, more obvious and rapidly developing negative changes in the body appear than in men.

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Introduction

In the modern world, cardiovascular pathology remains the main factor in the onset of disability, disability, and early death (Crea *et al*., 2015; Bespalov *et al*., 2018). Arterial hypertension (AH) is one of the most common diseases in the world that affects the heart and blood vessels (Alismail *et al.*, 2020). This pathology has recently been encountered more and more often in middle age and is considered a leading factor in the development of cardiovascular disorders (Karpov *et al*., 2020). The incidence of hypertension among residents of developed countries increases with increasing age. Middle-aged people have a 30% risk of arterial hypertension, while among people over 70 years of age, it is about 70% (Mills *et al*., 2016). The situation with AH is seriously aggravated by the fact that in the age structure of mortality from its complications, the prevalence of people of working age is traced (Fayzullina *et al*., 2020).

To the recommendations of the European Society of Cardiology / European Society of Hypertension, hemodynamic and metabolic changes, socioeconomic distress, and emotional overload are considered significant moments in the formation of arterial hypertension (Williams *et al*., 2018). The modern view of hypertension makes it necessary to seriously individualize the approach to its prevention and treatment (Alqahtani *et al*., 2021). This option of patient management is now considered the main one among many modern researchers, requiring it to take into account gender and individual characteristics (Minges *et al*., 2017).

Recent studies are beginning to focus on the presence of gender differences in cardiac patients, which were previously almost not taken into account (Al Zahrani *et al*., 2019). Much of the previous work has been done with only middle-aged men (Lee, 2017).

Undeniable facts are accumulating, pointing to differences between the sexes in the development of arterial hypertension, its course, and prognosis. A great vulnerability of the cardiovascular system was observed in the male part of the population. This is due to the high prevalence of arterial hypertension in mature men,



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often combined with overweight, smoking, and hypercholesterolemia (Jankauskiene & Baceviciene, 2019). For this reason, the first myocardial infarction in men is often recorded between 55 and 65 years of age, while among women it is recorded for the first time, usually at the age of 65-72 years (Kanic *et al*., 2016). Despite the importance of the problem of gender differences in hypertension, there are only a few studies devoted to the sexual characteristics of the development of hypertension, which dictates the need for in-depth research in this direction (Benjamin *et al*., 2017).

Objective

To trace gender differences in clinical and biochemical characteristics of patients suffering from hypertension in the first and second stages.

Materials and Methods

The work was performed at the clinical base of the Moscow State University of Medicine and Dentistry named after A. I. Evdokimov. All patients included in it, when taken under observation, gave voluntary informed written consent to their participation in the study. 80 patients of the second mature age (45-55 years) with confirmed hypertension were taken under observation, of which 44 patients had stage I hypertension and 36 patients had stage II disease.

Patients were divided into 2 groups according to their stage of AH. The first group with stage I AH included 11 men and 33 women. The second group with stage II arterial hypertension included 25 men and 11 women. Men and women of both groups were comparable in age. The criteria for inclusion in the study were the following signs: the presence of clinical manifestations of primary AH of I and II stages and the duration of hypertension for at least two years, the absence of concomitant diseases of the cardiovascular system, the absence of diabetes mellitus, the absence of acute forms or exacerbation of chronic inflammatory diseases, and the absence of cancer.

The clinical examination of all patients consisted of clarifying complaints, determining a gynecological history in women, a clinical examination consisting of an assessment of blood pressure, pulse, height, body weight, waist and hips, calculation of the Quetelet index - [body weight (kg)/height (m^2)]. In all cases, cholesterol levels were assessed; triglycerides; cholesterol included in lipoproteins having a high density; cholesterol included in lipoproteins having a low density; glucose; creatinine. In all those observed in plasma, by enzyme immunoassay using a kit manufactured by EnzoLifescience (USA), the amount of thromboxane B_2 and 6-keto-prostaglandin $F_{1\alpha}$ was recorded. Traditionally, the glomerular filtration rate was determined. In the course of Doppler ultrasonography, the thickness of the intima and media was determined in the wall of the common carotid artery (Elsheikh *et al*., 2020).

Statistical processing of the results of the study was carried out using the program Statistica 5.5. The arithmetic means and standard deviation (M±SD) were calculated for each indicator. The Student's t-test was used, and for paired comparisons of indicators within groups, the nonparametric Smirnov-Kolmogorov test was used. Differences were considered statistically significant at $p<0.05$.

Results and Discussion

The results of assessing the gender characteristics of the considered general indicators in patients suffering from stage 1 AH are presented in **Table 1**.

Table 1. General indicators of patients with AH of the first stage

Estimated indicators	Men, n=11	Women, n=33	Standard values
Age, years	49.1±11.43	51.6±7.08	-
Height, cm	176.8±3.06	168.4±5.34	-
The value of body weight, kg	82.8±10.15	73.7±14.31*	-
Body mass index, kg/m^2	26.5±3.16	27.3±4.64	<25
Waist, cm	91.0±5.61	83.3±11.73	<102for men, <88 for women
Hips, cm	102.2±2.87	106.3±10.36	-
Waist / Hip	0.88±0.05	0.78±0.06*	<0,9 for men, <0,85 for women
Systolic blood pressure, mm Hg	145.0±7.82	142.4±14.33	<140
Diastolic blood pressure, mm Hg	98.0±6.32	93.4±10.49	<90
Pulse beats / minute	68.2±7.96	78.4±10.71*	<80 per min
Glomerular filtration rate, ml / min / 1.73m^2	92.3±11.25	76.4±17.79*	>90
Intima-media complex thickness, mm	0.69±0.35	0.95±0.15	<0,9

Note: validity of differences between the sexes: * - $p<0.05$, ** - $p<0.01$. In the tables below the text, the designations are the same.

When comparing men and women suffering from stage 1 arterial hypertension by age and height, the comparability of the considered indicators was found. The body weight of men significantly exceeded the body weight of women in this group by 12.4%. At the same time, the body mass index in patients of different sexes in the group with stage 1 arterial hypertension did not differ. Their hips were comparable, and the waist tended to prevail in men. At the same time, the ratio of waist-to-hip volume in men significantly exceeded the same indicator in women by 12.8%.

The values of systolic and diastolic blood pressure were increased in both sexes to the level of arterial hypertension of the 1st degree with a certain tendency to prevail in men. At the same time, the pulse value in the group with stage 1 AH was 14.7% higher in women.

The glomerular filtration rate in patients with stage 1 AH demonstrated significant gender differences. In sick men, this indicator remained within the normal range. In women, it turned out to be reduced, yielding 20.8% less than the men's level. The thickness of the vascular intima and media in female patients slightly exceeded the normative level and significantly prevailed over the value of this indicator in men (by 37.7%).

The level of total cholesterol in the blood of patients with the first stage of arterial hypertension in both sexes exceeded the standard values with a tendency to prevail in women **(Table 2)**.

Table 2. Biochemical parameters of patients with AH of the first stage

Estimated indicators	Men, n=11	Women, n=33	Standard values
Total cholesterol, mmol/l	5.48±0.79	5.68±0.91	<5
Triglycerides, mmol/l	1.57±0.85	1.40±0.85	<1,7
The number of cholesterol lipoproteins with low density, mmol/l	3.18±0.67	3.96±0.83**	<3
High-density lipoprotein cholesterol, mmol/l	1.43±0.41	1.48±0.42	<1,0 for men, <1,2 for women
Glucose content, mmol/l	5.29±0.93	5.19±0.70	≤5,5
Creatinine level, mmol/l	84.4±8.11	79.2±18.54	<115 for men, <107 for women
Thromboxane B_2, pg/ml	174.2±0.52	182.9±0.64	<160
6-keto prostaglandin $F_{1\alpha}$, pg/ml	93.6±0.39	89.2±0.46	>95

The concentrations of triglycerides and cholesterol contained in high-density lipoproteins were comparable in patients of different sexes and were within the normal range. The amount of cholesterol in low-density lipoproteins in all patients was above the standard values.

At the same time, in women, its level was 24.5% higher than in men. The levels of glucose and creatinine in the observed patients remained within the normal range and had no gender differences. The concentrations of thromboxane and prostacyclin metabolites were outside the normative range. In the plasma of patients, the level of thromboxane B_2 was above the norm, and the amount of 6-keto-prostaglandin $F_{1\alpha}$ was inferior to the normative values. In women, their changes were somewhat more pronounced, forming a tendency towards a greater imbalance in the metabolites of arachidonic acid.

Gender characteristics of the considered general indicators of the group of patients suffering from stage 2 hypertension are presented in **Table 3**.

Table 3. Indicators of patients with arterial hypertension of the second stage

Estimated indicators	Men, n=25	Women, n=11	Standard values
Age, years	49.7±5.52	54.8±6.31	-
Height, cm	175.2±4.98	164.6±3.91	-
Body weight, kg	85.5±11.55	84.2±9.62	-
Body mass index value, kg/m²	27.9±2.98	31.3±3.15*	<25
The value of the waist, cm	94.8±6.82	95.7±11.66	<102 for men, <88 for women
Hips, cm	102.4±4.87	113.1±9.49*	-
Waist/Hip Ratio	0.93±0.07	0.85±0.05*	<0,9 for men, <0,85 for women
The value of systolic blood pressure, mm Hg.	156.0±12.33	163.3±18.72	<140

The value of diastolic blood pressure, mm Hg.	95.0±6.53	105.8±9.82*	<90
Pulse, beats / minute	66.5±9.05	68.8±7.09	<80 per min
Glomerular filtration rate, ml / min / 1.73m²	88.8±15.05	71.3±8.41**	>90
Intima-media complex thickness, mm	0.84±0.29	1.03±0.09**	<0,9

When comparing men and women suffering from stage 2 AH by age, body weight, and height, no significant differences could be found. The value of the body mass index in women with stage 2 hypertension exceeded the level of men by 13.3%. Women's hips were 11.0% larger, and the waist was comparable across the sexes. At the same time, the ratio of waist to hips in men significantly exceeded that in women by 10.0%.

Among patients with stage 2 hypertension, systolic and diastolic blood pressure values were increased in men to the level of 1 degree, and in women to the values of 2 degrees. The pulse value in the group with stage 2 AH was within the normal range for both sexes.

The plasma content of total cholesterol in patients with stage 2 AH of both sexes exceeded the standard values with a significant prevalence in women **(Table 4)**.

Table 4. Biochemical parameters of patients with second-stage hypertension

Estimated indicators	Men, n=25	Women, n=11	Standard values
Level of total cholesterol, mmol/l	5.3±0.93	6.3±1.53*	<5
Triglycerides, mmol/l	1.36±0.98	1.49±0.38	<1,7
Cholesterol of lipoproteins with low density, mmol/l	3.29±0.88	3.36±0.26	<3
High-density lipoprotein cholesterol, mmol/l	1.23±0.34	1.31±0.27	<1,0 for men, <1,2 for women
Glucose content, mmol/l	5.28±0.49	5.19±0.47	≤5,5
Creatinine, mmol/l	89.6±13.73	83.8±9.43	<115 for men, <107 for women
The amount of thromboxane B_2, pg/ml	179.4±0.48	188.7±0.73	<160
Level of 6-keto-prostaglandin $F_{1\alpha}$, pg/ml	90.8±0.35	83.6±0.42	>95

The concentrations of triglycerides and cholesterol found in high-density lipoproteins were comparable in patients of different sexes and were within the normal range. The content of low-density lipoprotein cholesterol in the blood was comparable to the normal level in patients of both sexes.

Blood glucose and creatinine concentrations in all patients with stage 2 AH were within the normal range and did not differ in different sexes. The levels of thromboxane and prostacyclin metabolites in all examined patients were beyond the normative values. In women, violations of their levels tended to be more pronounced, forming a tendency to a more pronounced imbalance in their blood of arachidonic acid metabolites.

The glomerular filtration rate in patients with stage 2 AH showed significant gender differences. In sick men, this indicator was slightly below the norm, while in women it was significantly reduced, yielding to the level of men by 25.0%. The thickness in the vessels of the intima and media in women with stage 2 AH exceeded the normative level and prevailed over the value of this indicator in men by 23.0%.

Various aspects of AH have been studied for a long time (Mehta *et al*., 2016). This is carried out both in the clinic and in the course of various experiments (Kotova *et al*., 2017). The main invariable risk factors for the development of hypertension are known - gender and age (Zavalishina *et al*., 2018). At the same time, most researchers note that the incidence of hypertension increases with increasing age (Mendelsohn & Karas, 2005). At the same time, the study of gender characteristics in the development and course of AH was started not so long ago. For the first time in the Framingham Heart Study, it was possible to find clear differences between hypertensive patients of different sexes. It is noticed that up to 50 years of age AH affects men more often. At an older age, the incidence of this disease increases in women, which is associated with an increase in the number of factors contributing to the development of hypertension in them (Liu *et al*., 2001; Stramba-Badiale *et al*., 2006).

The authors of this work found that in hypertensive patients with stage 1 AH in men, by the age of 49 years, higher numbers of systolic and diastolic blood pressure began to be noted compared to women. Their mean age of manifestation of hypertension was 51 years. The average age of registration for stage 2 AH in women was about 55 years. In hypertensive men, this age was 50 years. At the same time, in AH of the second stage, the blood pressure figures were higher in the female part of the observation group.

Being overweight and especially obese are strongly associated with an increased risk of numerous pathological conditions, including dyslipidemia, type 2 diabetes mellitus, metabolic syndrome, and focal segmental glomerulosclerosis (Aleksandrovna & Zavalishina, 2017). The authors noted that in patients with the first stage of AH in both sexes, there was a tendency to increase the body mass index. In women with the second stage of AH, the body mass index reached 30, while in men this indicator remained practically unchanged. The data obtained can be explained by hormonal changes in the body of a woman, which can increase the amount of body weight, leading to the appearance of abdominal obesity (Gallego *et al*., 2015; Karvonen-Gutierrez & Kim, 2016).

Metabolic risk factors for the occurrence of cardiovascular and metabolic disorders are recorded much more often in hypertension than in normatonic patients. Researchers have recently placed particular emphasis on waist circumference and waist-to-hip ratio, with less emphasis on body mass index. These indicators can more accurately indicate the appearance of abdominal obesity (Zavalishina, 2020). The authors found that in the case of the first stage of AH in both sexes, the waist volume remained within the normal range. However, in the course of the observation, it was noted that the ratio of the waist to the volume of the hips turned out to be greater in men, going beyond the normal range. In women with stage 2 AH, the waist volume and the ratio of waist to the hip volume were more than normal. In males, the average values of waist volume were not greater than the threshold values. The value of the ratio of the volume of the waist to the volume of the hips did not exceed the normative level but was less than this value in women. The information obtained does not contradict the available information that with an increase in blood pressure, the ratio of waist volume to hip volume increases (Minges *et al*., 2017).

Earlier work revealed that there is an undoubted connection between the increase in the concentration of triglycerides, total cholesterol, low-density lipoprotein cholesterol, and the risk of atherosclerosis manifestation. For the blood level of high-density lipoprotein cholesterol, this relationship is negative (Williams *et al*., 2018). The authors were able to show the comparability of total cholesterol levels in patients of both sexes with the first and second stages of AH. At the same time, all found concentrations of total cholesterol were above the normative level. Triglyceride concentrations showed a different pattern. Their average levels in patients of both sexes with the first and second stages of AH were within the generally accepted norm

When analyzing data on the level of low-density lipoprotein cholesterol, in the group with AH of the first stage, women showed a significantly higher content than men. In the second stage of AH, no differences in atherogenic low-density lipoprotein cholesterol were found between the sexes. The modern concept of the mechanism of atherosclerotic plaque formation in accordance with the lipid-infiltration theory assumes the entry into the subendothelial space of native and oxidized molecules, low-density lipoproteins. Moreover, the higher their level in the blood, the more intensively this process always proceeds. Consequently, women are highly susceptible to the rapid progression of atherosclerosis in the formation of hypertension.

In the work carried out in patients with the first stage of AH, a comparable concentration of high-density lipoprotein cholesterol in men and women was determined. In the group observed with hypertension in the second stage, no significant differences were also obtained. The level in patients with the second stage of AH was lower than in the first stage but did not decrease to the threshold level for high-density lipoprotein cholesterol.

In terms of glucose, the reliability of gender differences was not obtained in patients with the first stage of AH and patients with the second stage of AH. This indicates the maintenance of carbohydrate metabolism at a normal level in all examined patients.

When assessing the glomerular filtration rate, it was possible to obtain the reliability of the differences in this indicator between the sexes in both comparison groups. Mean values in men were significantly higher in the first stage of AH and in the second stage of AH. This allows us to say that women with hypertension are prone to earlier development of chronic kidney disease. It is known that estrogen has an antiproliferative effect on smooth muscle cells, and progesterone lowers the tone of arterioles and reduces sodium resorption in the renal tubules, thereby exerting an anti-mineralocorticoid effect. The loss of the optimal level of these hormones in postmenopausal women inevitably leads to the deterioration of renal function (Hodis *et al*., 2003).

At the same time, more pronounced disturbances in the synthesis of biologically important substances that can stimulate the aggregation of blood cells were noted in women with hypertension in platelets and vessel walls. In women with AH, the level of blood proaggregants pronouncedly increased as the disease progressed compared to the men. The greater intensification of thromboxane synthesis that develops in women, combined with a greater weakening of the formation of a substance with the opposite effect - prostacyclin, creates a more pronounced imbalance in the plasma between the activity of antiplatelet agents and substances - proaggregants. It can be thought that the violation of the ratio of arachidonate derivatives, which is created in AH, creates more pronounced conditions for microrheological disorders in women, starting from stage 1 of AH.

According to the definition of the World Health Organization, atherosclerosis is called "a variable combination of changes in the intima of the arteries, including the accumulation of lipids, lipoproteins, complex carbohydrates, fibrous tissue, blood components, calcification in the middle membrane of the vascular wall." It is recognized that in the walls of the arteries in patients with hypertension under the influence of pressure loading, there is a gradual increase in the thickness of the intima and media of the vessels, associated with the progression of atherosclerosis (Finn *et al*., 2010). According to the known data on the presence of asymptomatic target organ lesions in AH, it is appropriate to speak about the presence of subclinical atherosclerosis in a patient with AH (thickness of the intima/media complex> 0.9 mm).

The world medical science recognizes the presence of gender differences in the formation of atherosclerotic vascular lesions, caused, first of all, by the peculiarities of the influence of the existing endocrine profile on the body (Monleiro, 2005). Estrogens slow down the remodeling of large arteries and inhibit the accumulation of foam cells in the vascular wall. They are also able to reduce the stiffness of the arterial wall and the magnitude of arterial systolic pressure by relaxing smooth myocytes in the walls of blood vessels. Progesterone also lowers the tone of arterioles and inhibits the proliferation of smooth muscle coronary arteries due to the blockade of slow calcium channels in their walls (Bots *et al*., 1994; Bonithon-Kopp *et al*., 1996).

In the study, men with the first stage of AH showed significantly lower values of the part of the intima-media of the vessels compared with women with stage 1 AH. In the group with AH of the second stage, men again demonstrated a significantly lower value of the intima-media complex index than women. The data obtained are consistent with previously published works, where in premenopausal patients a positive relationship was found between an increase in the thickness of the intima-media complex of the carotid common artery and an increase in the level of pulse pressure, triglyceride levels, body mass index, and age (Fröhlich *et al*., 2004). Thus, according to the information found in our study, it can be assumed that the examined men do not have, and the women taken under observation have subclinical atherosclerosis.

Considering the state of metabolic parameters in patients with hypertension, one can think that they had excessive body mass indices, indicating the presence of obesity in combination with lipid metabolism disorders to the level of atherogenic dyslipidemia (Lobo, 2017). Changes in metabolism are already present at the onset of arterial hypertension in women. This is consistent with the point of view of a decrease in the severity of the cardioprotective effect of estrogens during premenopause.

Conclusion

Arterial hypertension is a very common disease globally. The prevalence of hypertension increases with age. Its presence always aggravates the work of the cardiovascular system, accelerating the development of atherosclerosis. Worldwide, hypertension is an important factor in disability, disability, and death in patients of both sexes. Taking into account sex differences makes it possible to reveal the gender characteristics of the values of pathogenetically significant indicators in patients with arterial hypertension. There is reason to believe that from the very beginning of the development of AH in women, more pronounced and more rapidly progressive lipid, hemostatic, and renal disorders occur in comparison with men. This significantly worsens their prognosis and requires more attention from clinicians for women with hypertension.

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