

**The aim** was to determine the effect levels of thyroid stimulating hormone (TSH) on frequency and severity of cardiovascular risk factors in hypertensive patients.

**Material and methods of the research.** The study included 123 people with stage 2 hypertensive disease, grade 2 arterial hypertension (AH). The patients' age averaged  $66.08 \pm 8.7$  years (from 45 to 75 years). The duration of AH was  $15.6 \pm 6.2$  years. 96 (74%) of women and 33 (26%) men participated in the research. 28 (29.2%) women were younger than 60; 68 (70.8%) older than 60. 10 (35.0%) men were younger than 60 and 23 (65.0%) older than 60. People included in the study were divided into two groups depending on thyroid function condition. 16 patients with concomitant subclinical hypothyroidism (SH) were included in the first group; the second group had 107 patients without SH. Patients with SH were 12.4% of all the patients, which is not different from population data presented in the literature. Subsequently, the second group has been divided by the level of TSH into two subgroups with high-normal (from 2.0 mU/l to 4.0 mU/l) and low-normal (0.4 mU/l to 2.0 mU/l) TSH levels, which included 54 and 53 patients accordingly. The groups were matched together according to age, sex, duration of AH, baseline levels of systolic blood pressure (SBP), diastolic blood pressure (DBP) and heart rate. Additionally, the division of patients into two groups by age into group of middle-aged (45 to 60 years) and elderly group (60 to 75 years) was conducted.

Therefore, a group of elderly people was divided into three subgroups by TSH level: first subgroup consisted of patients with SH (15 persons); second subgroup included patients with low-normal TSH level (41 persons); third subgroup had patients with high-normal TSH level (20 persons). Average age group has been divided into two subgroups: the first subgroup had patients with low-normal TSH level (20 persons); second subgroup contained patients with high-normal TSH level (15 persons), because among middle age group there was only 1 person with SH.

The studies as anthropometric (height, weight, body mass index (BMI), waist measurement, general clinical researches, including measurement of blood pressure (BP), 12-lead ECG, ambulatory blood pressure monitoring and ECG, echocardiography with calculation of parameters of intracardial and systemic hemodynamics, duplex scanning of neck vessels, testing by Hamilton scale (depression grade), A.M. Vein questionnaire,

assessment of quality of life by the visual analogue scale (VAS), ultrasound of abdomen and thyroid, laboratory methods were conducted. Along with the general and biochemical blood analysis and definition of lipid panel TSH level and thyroid hormones, creatinine (glomerular filtrate rate (GFR) calculation by CKD-EPI formula), albumin-creatinine ratio in urine were determined.

**Results.** In the first phase of the study anthropometric data in groups with and without SH were compared. The average weight of patients in SH group was  $77.93 \pm 2.77$  kg and group without SH was  $84.56 \pm 0.78$  kg,  $p < 0.05$ . Average height in SH group was  $1.61 \pm 0.02$  m, and in group without SH was 1.66 m,  $p < 0.05$ . BMI, waist-to-hip ratio (WHR) did not have significant difference in the groups.

Office blood pressure measurement was performed all patients according to European Society of Hypertension (ESH) and the European Society of Cardiology (ESC) clinical recommendations for AH in 2013 [4]. During the study of office blood pressure we discovered that systolic blood pressure (SBP) in SH group was significantly higher compared with people without SH. It concerned people with low-normal and high-normal TSH levels. The difference in SBP was 10-14 mm Hg and it was the largest in group with low-normal TSH level. The average indices of diastolic blood pressure (DBP) in SH group were not much higher than those in other groups; the difference was 4-5 mm Hg and it was not reliable. Accordingly, the pulse blood pressure (PBP) was significantly higher in SH group compared to all other groups, including a group of high-normal TSH level.

Along with the level of SBP and PBP disturbed blood pressure profile of the examined people plays certain role in the deterioration of prognosis. By the results of ambulatory blood pressure monitoring (ABPM) day blood pressure profile of patients in the studied groups has been identified. SBP day profile in AH+SH group was characterized by the fact that 50% were non-dipper, i.e. half of patients with SH had not sufficient night SBP reduction.

There were 7% less non-dippers in the group of patients with AH without SH profile. The level of TSH in patients without SH is important. In the group with TSH high-normal level of non-dipper was 46%, and a group of low-normal TSH level of non-dipper was 40%. ABPM profile of non-dipper group with SH was 33%, and it is more than 10% in the

group with AH without SH, 21% more than in the group with high-normal TSH level and 22% more than in the group with low-normal TSH level.

In the study of frequency of dyslipidemia was revealed that high cholesterol group AH+SH occurred 10% more compared with AH without SH group, increased cholesterol of low-density lipoprotein (LDL) > 3.0 – 10% more, lower cholesterol LDL <1.0 – 6% more compared with AH without SH group. Regarding frequency of hypertriglyceridemia in two groups there was no significant difference. It should be noted that inclusion in the study, patients in both groups received statins occasionally, regularly, made long breaks.

Among elderly people with low-normal TSH level was 57%, with high-normal was 22%, with SH was 21%. Among middle-aged people with low-normal TSH level was 54%, with high-normal was 43%, with SH was 2.8%. First a comparison of anthropometric indicators in elderly groups with different levels of TSH was carried out.

After the analysis of elderly patients with different TSH levels, there were found that patients with low-normal TSH level (Group 2) average indicators of body weight, waist ratio and BMI were significantly higher compared with patients with 1<sup>st</sup> and 3<sup>rd</sup> groups and patients with obesity in this group appeared to 2% more than in the 1<sup>st</sup> and 4.8% more than in the 3<sup>rd</sup>.

Then there was the comparison of anthropometric parameters between two groups of middle-aged patients with low-normal and high-normal TSH levels and relevant groups of elderly patients.

In the analysis of these data significantly higher percentage of obesity in middle-aged group with high-normal TSH level compared to low-normal (74% vs. 40%,  $p < 0.05$ ) was found. In older patients with low-normal TSH level percentage of people with normal BMI was significantly greater than in the group with high-normal TSH level.

As important markers that determine prognosis in patients with AH are recognized such signs of subclinical target organ damage as myocardial hypertrophy, albuminuria, increased PBP > 60 mm Hg and ultrasound signs of carotid arteries damage in the form of increase in "intima-media thickness" and atherosclerotic plaques. We compared the frequency of existing left ventricle hypertrophy and other target organ damage in groups AH+SH and AH without SH.

In group with AH+SH was detected a relatively higher percentage of patients with left ventricle hypertrophy, increased PBP, but the difference was not significant. The percentage of atherosclerotic carotid disease in the group AH+SH was significantly greater according to literature data. It matches with our data on the greater frequency of dyslipidemia in patients with concomitant AH and SH. Further various factors of cardiovascular risk, incidence of target organ damage and diabetes mellitus (DM) in our patients, divided into 5 groups according to age and level of TSH were analysed. In older people with SH left ventricular hypertrophy (LVH) occurs significantly more often. This can be associated with higher parameters of SBP and PBP. The highest percent of LVH was determined in group AH+SH (87%); 12% less in group of elder patients with high-normal TSH level (75%); 50% less in group of middle-aged patients with low-normal TSH level (37%). The index in groups of middle-aged and elder patients was 33% and 37% accordingly. Eccentric hypertrophy prevailed in all groups. Concentric hypertrophy was revealed only in groups with SH (14%) and high-normal TSH level (9%).

We conducted the testing by Anxiety and Depression Scale (HADS), A.M. Vein questionnaire, assessment of quality of life by the visual analogue scale (VAS). According to quality of life VAS data (with the assessment of patients' health state from 0 to 100 at the time of examination) the percentage of patients with more than 50 points in groups was as follows: in group with AH+SH it made up 37.5% (6 persons), in group with AH without SH – 35.5% (38 persons). No possible differences were found.

Compared to the groups with low-normal TSH level ( $6.01 \pm 0.33$  mmol/l) and high-normal TSH level ( $5.3 \pm 0.29$  mmol/l,  $p < 0.05$ ) possible increase of urea in group with AH+SH was found. This confirms the negative impact of SH on kidney function in patients with AH. The other average values of laboratory indexes did not have possible differences. Laboratory indices in patients of different age with AH depending on TSH level in blood were analysed. There were no possible differences between indices of biochemical blood analysis between groups with low-normal and high-normal TSH level.

Analysis of the prevalence of risk factors, organ - targets damages, blood pressure values and its daily profile in patients with AH depending on the condition of thyroid function allowed us to make the following conclusions.

**Conclusions.** Among the examined outpatients with AH frequency SH was 12.4%, which is different from the general population data. In the group of elderly patients with low-normal TSH level was 57%, with high-normal – 22%. In the group of middle-aged people with low-normal TSH level was 54%, with high-normal – 43%. Prevalence of SH and its value in increasing cardiovascular risk requires the practitioner examination of patients with AH on indicators of thyroid function, not just thyroid ultrasound.

The presence of subclinical hypothyroidism has a negative impact on lipid and carbohydrate metabolism; in the SH group was found a higher percentage of patients with factors of cardiovascular risk (total cholesterol > 4.9 mmol/l, LDL cholesterol > 3.0 mmol/l, HDL cholesterol <1.0 mg/l and TH > 1.7 mmol/l, increased fasting glucose level). Thus the average values of these parameters in groups with and without SH have no difference, requiring an individual assessment of cardiovascular risk in the population of people with SH, which demonstrates the role of the state in the accompanying deterioration of prognosis in cardiac patients.

The presence of SH worsens target organ damages in patients with AH, namely – SH group has the highest percentage (94%) of people with LVH and atherosclerotic lesions of the carotid arteries, which leads to increased overall cardiovascular risk in people of middle and elderly age. The frequency of atherosclerotic carotid arteries damage may be associated with lipid metabolism.

High-normal TSH level is connected with the deterioration of target organs condition and increase of cardiovascular risk factors in patients with AH of middle and elderly age. Thus, a group of elderly high-normal TSH levels had a significantly higher percentage of patients with low levels of HDL, high LDL levels, increased fasting blood glucose levels compared with a group of low-normal TSH level. Group of middle age with high-normal TSH level had significantly higher percentage of patients with low levels of HDL and increased levels of TH and significantly higher percentage of patients with LVH compared with the corresponding age group of low-normal TSH level. When comparing the groups with high-normal TSH levels in middle and elderly age the incidence of pathological changes was greater in the second group, indicating that the negative impact of age-related

changes at the same time requires careful monitoring of thyroid function in older people with AH.

In AH patients with TSH level effect on BMI depend on age. Thus, in elderly patients SH impact and state with high-normal TSH level on body mass index less marked than in middle age patients. Overall, the substantial connection of SH and TSH level within the referent values with obesity and overweight is not stated, so SH does not impact on risk factors through weight gain.

The presence of SH is associated with reduced GFR in patients with AH of middle and old age, which may indicate the role of the state in the progression of chronic kidney disease. It requires a doctor monitoring kidney function in people with hypothyroidism and control of thyroid function in patients with lesions of kidney including with AH.

The presence of SH negatively affects the psychological and emotional state associated with increased frequency of depression in patients with AH, the frequency of vegetative dysfunction that may be displayed on control blood pressure.

In patients with AH a direct correlation relationship between TSH and BMI ( $r = 0.46$ ,  $p < 0.05$ ), between TSH and total cholesterol and LDL ( $r = 0.87$ ,  $r = 0.84$  respectively,  $p < 0.05$ ), between TSH and fasting blood glucose levels ( $r = 0.81$ ,  $p < 0.05$ ); as well as the inverse relationship between TSH and GFR ( $r = 0.46$ ,  $p < 0.05$ ) is identified. It may indicate the reduction of the role of thyroid function in increasing frequency and severity factors of cardiovascular risk and target organ damages in case of AH. Therefore, the control of thyroid condition in patients with AH and high cardiovascular risk should be obligatory.