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O.N. Antropova, S.B. Silkina, I.V. Osipova PREDICTORS OF THE DEVELOPMENT OF HYPERTENSION IN YOUNG PEOPLE WITH HIGH NORMAL BLOOD PRESSURE

Aim: to identify predictors of the development of arterial hypertension (AH) in young people with high normal blood pressure (HNP) based on the study of risk factors, hemodynamic parameters, structural and functional parameters of target organs. 155 patients under 45 years of age were included, mean age 35.1±3.2 years. Taking into account the indicators of office and ambulatory blood pressure (BP), the distribution into groups of HNP (68 patients) and AH (87 patients) was carried out. Conducted general clinical, laboratory, functional examination. Daily BP monitoring was performed for 24 hours using the BpLAB device (LLC Petr Telegin) with the integrated Vasotens® system, which makes it possible to evaluate central BP along with BP in the brachial artery. A complex of factors that increase the risk of developing hypertension in young people with HNP has been identified. Among them are hemodynamic, a number of risk factors (increased very low density lipoprotein cholesterol, triglycerides, total cholesterol, low density lipoprotein cholesterol, smoking experience, body mass index and waist circumference, age), intima-media thickness of brachiocephalic vessels, LA dimensions.

Keywords: arterial hypertension, high normal blood pressure, developmental predictors, young age.

Introduction. Numerous studies demonstrate that high normal blood pressure (HNP) is an independent risk factor (RF) for the development of cardiovascular disease (CVD). Patients with HNP have a higher risk of developing arterial hypertension (AH) than patients with optimal blood pressure (BP) [4]. The data obtained in the epidemiological study Framingham Heart Study revealed the formation of hypertension in HNP and normotensive profile in 54.2% and 23.6%

in men and in 60.6% and 36.2% (respectively in HNP and normal blood pressure) in women . Thus, the risk of AH in baseline HNP increased by 2.25 times (p<0.0001) in men and by 1.89 times in the female population (p<0.0001) [8]. According to Y. Ishikawa et al. in a prospective cohort study conducted in Japan, it was shown that after 11 years, 26.1% of persons with prehypertension developed AH, the risk of developing AH in persons with VNP was 3.57 times higher than in persons with normotension [5].

The combination of several RFs contributes to the earlier progression of VNP to AH. Thus, the results of an American study involving more than 30,000 patients showed that in individuals with VNP and three RFs, the appearance of stable AH was noted for 4 years [1]. In a Korean cohort study that included patients with a normotensive status and prehypertension, the main predictors of the transformation of HNP into AH were: hypercho-

lesterolemia, hyperglycemia, hyperuricemia, smoking, age, and an early family history of hypertension [7]. In another study, ethnicity, older age, higher body mass index (BMI), and the presence of diabetes or chronic kidney disease were independently and positively associated with the development of hypertension [11]. It should be noted that the studies included either adolescents or patients of older age groups; there are no data on predictors of hypertension in patients under 45 years of age. In addition, a complex of factors possibly associated with the development of AH has not been previously studied: hemodynamic, behavioral, structural and functional.

The aim of the study was to identify predictors of the development of arterial hypertension in young people with high normal blood pressure based on the study of risk factors, hemodynamic parameters, structural and functional parameters of target organs.

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Material and methods. On the basis of the consultative polyclinic department No. 2 of the Diagnostic Center of the Altai Territory and the therapeutic department of the National Healthcare Clinical Hospital at the Barnaul station in 2015-2020. 155 patients were examined. The inclusion criteria for the study were: age from 20 to 45 years; the presence in patients of the criteria for hypertension or VNP according to the anamnesis and measurements of office blood pressure; informed consent of the patient; lack of regular intake of antihypertensive drugs. The average age of the subjects was 35.1±3.2 years. Taking into account the indicators of office and ambulatory blood pressure, the distribution into groups of VNP and AH was carried out. Depending on the indicators of office BP, patients were divided into groups according to the level of office and daily BP according to the current classification (ESC 2018): the second with hypertension (with blood pressure of 140/90 mm Hg or more). In 4 patients who met the criteria for VNP according to the level of office BP, a masked form of AH was detected and these patients were assigned to the AH group. Thus, the number of patients with HNP was 68 people (mean age 33.1±7.5 years), the group with AH consisted of 87 people (mean age 36.4±6.6 years).

During medical appointments, patients were assessed body mass index (BMI), waist circumference, office assessment of blood pressure, heart rate. The levels of glucose in blood serum samples, total blood cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), triglycerides (TG), uric acid, creatinine were determined with the calculation of glomerular filtration rate (GFR) according to the formula CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration), daily albuminuria. Daily blood pressure monitoring was carried out for 24 hours using the BpLAB device (LLC Petr Telegin) with the integrated Vasotens® system, which allows to evaluate central blood pressure along with blood pressure on the brachial artery: mean systolic and diastolic blood pressure (SBP and DBP) average daily, in daytime and nighttime, mean pulse BP, degree of nocturnal decrease in SBP and DBP, amplification index and augmentation index. Echocardiography was performed using the EnVisorC device from Philips (Holland) with a 3.5 MHz transducer according to the standard technique. Ultrasound examination of brachiocephalic vessels (BCV) was performed using an EnVisor C ultrasonic device from Philips (Holland)

Predictors of the development of arterial hypertension

Predictor	OR [95% ДИ]	р
Гемодинамические факторы		
Systolic blood pressure on the aorta at night	2.06 [1.38; 4.47]	0.010
Systolic blood pressure on the aorta daily allowance	1.55 [1.23; 2.31]	0.004
Systolic blood pressure on the aorta afternoon	1.4 [1.17; 1.83]	0.002
Pulse blood pressure on the aorta	1.11 [1.02; 1.26]	0.046
Systolic blood pressure	1.49 [1.18; 2.32]	0.014
Diastolic blood pressure	1.34 [1.13; 1.76]	0.006
Systolic blood pressure on the brachial artery at night	1.2 [1.11; 1.32]	< 0.001
Systolic blood pressure on the brachial artery afternoon	1.16 [1.09; 1.26]	< 0.001
Diastolic blood pressure on the brachial artery at night	1.15 [1.07; 1.26]	0.001
Risk factors		
Very low lipoprotein cholesterol	4.24 [1.63; 12.27]	0.005
triglycerides	2.02 [1.24; 3.46]	0.007
Total blood cholesterol	1.9 [1.35; 2.77]	< 0.001
Low-density lipoprotein cholesterol	1.82 [1.2; 2.84]	0.007
Smoking history	1.34 [1.11; 1.77]	0.011
Body mass index	1.1 [1.03; 1.18]	0.007
Waist circumference	1.05 [1.02; 1.08]	0.003
Age	1.09 [1.03; 1.15]	0.002
Structural indicators of target organs		
Left ventricular myocardial mass index	3.25 [1.36; 8.69]	0.012
Left atrium	9.41 [3.37; 29.74]	< 0.001
Intima media thickness	11.35 [1.58; 107.42]	0.023

Note: The results of the calculations are shown in the tables as indicators of the odds ratio (OR) of adverse events (AH) in individuals with VNP to increase the indicators by 1 unit of measurement. The table also shows estimates of the significance level p, which is calculated in the program through standardized statistics z for the coefficients of the model.

with a linear scanner for surface studies. During this examination, the thickness of the intima-media complex (ITM) of the carotid arteries in the areas of carotid bifurcations and in the area of the common carotid arteries was determined.

Statistical calculations were carried out in the RStudio program (version 1.2.5001 - © 2009-2019 RStudio, Inc., USA, URL https://www.rstudio.com/) in R language (version 3.6.1, URL https:// www .R-project.org/). Empirical distributions of data were tested for agreement with the law of normal distribution according to the Shapiro-Wilk test. The nonparametric Mann-Whitney U-test was used to compare scores between groups. For statistical testing of hypotheses about the equality of the numerical characteristics of sample distributions in the compared groups, the unpaired Mann-Whitney U-test was used, the distribution bias was calculated with the construction of a 95% confidence interval for the bias. The identification of AH predictors was carried out by building logistic regression models. Statistical hypotheses were tested at a critical significance level p = 0.05, i.e. the difference was considered statistically significant if p < 0.05.

Results and discussion. By constructing single-factor logistic regression models, individual predictors of hypertension were identified (Table 1). Among the hemodynamic variables, the increase of which by 1 mm Hg. was associated with an increase in the chances of hypertension, indicators of daily monitoring of central blood pressure: SBP at night (by 2.06 [1.38; 4.47] times) and daytime hours (by 1.4 [1.17; 1.83] times), average daily (by 1.55 [1.23; 2.31] times) and pulse central pressure (by 1.11 [1.02; 1.26] times). An increase in office SBP (by 1.49 [1.18; 2.32] times) and DBP (by 1.34 [1.13; 1.76] times) and BP monitoring indicators on the brachial artery was associated with the risk of hypertension: SBP at night (by 1.2 [1.11; 1.32] times), SBP in the daytime (by 1.16 [1.09; 1.26] times), DBP at night (by 1.15 [1.26] times). 07; 1.26] times).



Risk factors were identified, the increase of which was associated with the risk of AH: increased VLDL cholesterol (OR 4.24 [1.63; 12.27]), triglycerides (OR 2.02 [1.24; 3.46]), total cholesterol (OR 1.9 [1.35; 2.77]), LDL cholesterol (OR 1.82 [1.2; 2.84]), smoking history (OR 1.34 [1.11; 1.77]), body mass index (OR 1.1 [1.03; 1.18]) and waist circumference (OR 1.05 [1.02; 1.08]), age (OR 1.09 [1.03; 1.15]). The most significant predictors of the development of AH in individuals with VNAD were: IMT of brachiocephalic vessels (OR 11.35 [1.58; 107.42]), left atrial size (OR 9.41 [3.37; 29.74]) and LVH (OR 3.25 [1.36; 8.69]

By constructing a multivariate logistic regression model, significant predictors of AH were identified that act multiplicatively: LA diameter (p = 0.006), an increase in LA diameter by 1 cm is associated with an increase in the chances of AH by 6.43 [1.84; 26.43] times; total cholesterol (p = 0.014), an increase in the indicator by 1 mmol/l is associated with an increase in the chances of AH by 1.75 [1.14; 2.81] times.

The identification of risk factors for the progression of hypertension in a population of young patients with VNP is more informative than a simple comparison of hypertensive and normotensive groups, because it may actually reflect which risk factors need to be identified and managed. The heterogeneity of the hemodynamic picture at a young age determines a different prognostic scenario. Of particular interest is associated with young patients, since the role of an isolated increase in blood pressure in this category of individuals is currently being discussed. Some studies have shown that isolated systolic hypertension (ISAH) in young people is a "false phenomenon" [3], while others, on the contrary, have concluded that it is associated with increased cardiovascular risk [10]. The results of our study showed that an increase in both office SBP and DBP has approximately the same predictor significance. In addition, 24-hour brachial BP monitoring does not have a significant advantage over office measurements in assessing the odds ratio of developing AH in individuals with VNP. The value of central BP as a significant predictor of new onset hypertension after 4 years of follow-up was previously determined in a study of 7840 subjects with normal BP (mean age 51 years) (P<0.001) [12]. Our results also identify central BP as a

significant tool for predicting the risk of hypertension.

Obviously, the development of hypertension is due not only to the hemodynamic profile, but also to the multifactorial nature of the increase in blood pressure. When studying risk factors, we identified predictors of the development of hypertension in young people with VNP: dyslipidemia, smoking, obesity, and age. Attention is drawn to the association of the development of AH with the indices of the lipid spectrum and the thickness of the intima-media of the brachiocephalic vessels. This relationship is based on several pathogenetic mechanisms: endothelial dysfunction, oxidative stress and vascular inflammation, activation of the renin-angiotensin system [6].

It is noteworthy that the diameter of the left atrium was a predictor of the development of AH not only in univariate, but also in multivariate analysis. Atrial dilatation occurs when an increase in filling pressure leads to stretching of the walls of the chamber of the heart. The role of an increase in the structural and volume parameters of LA in the development of CVD, in particular atrial fibrillation and heart failure, including diastolic, is known. In a previous meta-analysis of 20 echocardiographic studies, it was shown that in individuals with VNP, in comparison with individuals with normal blood pressure, an increase in the diameter of the left atrium is determined [2]. Our study demonstrated data supporting an association of increased AH risk with left ventricular myocardial mass index in young patients with VNP. These data are consistent with a previous study by Chinese authors, which included 10,547 patients with hypertension, prehypertension, and normotensives, and showed that the prevalence of left ventricular hypertrophy was statistically different between the three groups (p<0.001); SBP, DBP, and mean SBP were independent risk factors for structural changes in the left heart [9].

Conclusion. A complex of factors that increase the risk of developing hypertension in young people with VNP has been identified. Among them are hemodynamic (SBP and DBP, determined by monitoring the central and brachial, office measurement), clinical (VLDL cholesterol, total cholesterol, LDL cholesterol, smoking experience, body mass index and waist circumference, age). The thickness of the intima-media of the brachiocephalic vessels, the size of the left atrium and LVH were significant predictors of the development of AH in individuals with VNP. The multivariate model shows the predictor value of the diameter of the left atrium and total cholesterol.

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