ASSESSMENT OF POLYGENIC RISK OF ARTERIAL HYPERTENSION

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Arterial hypertension (AH) is a leading risk factor for the development of cardiovascular diseases. In recent decades, the rapid development of genetic research, in particular genome-wide association search (GWAS), has made it possible to identify hundreds of variants of the nucleotide sequence associated with the development of hypertension. One of the approaches to improving the predictive ability of genetic testing is to combine information about many variants of the nucleotide sequence into a single risk assessment system, often called the genetic risk scale. Within the framework of this review, the most significant publications on the study of the AH genetic risk scale will be considered, the features of their development and application will be discussed.

Key words: *arterial hypertension, genetic risk scale.*

Introduction. The prevalence of arterial hypertension (AH) in the world is 1.28 billion people1. It is the leading risk factor (FR) for the development of cardiovascular diseases (CVD) - coronary heart disease (CHD), myocardial infarction, stroke, heart failure, peripheral atherosclerosis and atrial fibrillation, and also leads to damage to target organs [1]. It is known that the development of hypertension at a young age in parents is associated with its early development in offspring [2], and according to the results of twin studies, the heritability of hypertension is 50-60% [3]. However, this indicator, based only on the patient's survey, is not sensitive enough [4].

It is a multifactorial disease, the genetic basis of which includes many polymorphic loci. Thus, using a full genomic association search (GWAS), >900 loci and >1000 variants of the nucleotide sequence (GNP) associated with the development of hypertension were identified [6, 7]. However, each individual genetic variant has a weak influence on the development of hypertension, explains a very small proportion of heritability in the development of the disease and, thus, has limited predictive value. One of the solutions to increase the predictive ability of genetic testing is to combine information about several GNPs into a single risk assessment system, often called the "genetic risk scale" [8]. At the population preventive level, this approach will make it possible to identify among young people a group at increased risk of developing hypertension and implement more in-depth programs of preventive measures for it [9]. Such a targeted approach assumes that the earlier the modifiable FR is corrected, the more effective the prevention of CVD is [10]. Thus, the identification of high-risk groups of hypertension seems to be an extremely urgent task. Non-drug approaches to blood pressure control (BP) (reducing the use of sodium chloride and sufficient intake of potassium and other elements, maintaining a normal weight, limiting alcohol consumption and regular physical activity) can reduce

systolic blood pressure (SAD) by ≥10 mmHg [11-13]. This degree of reduction in blood pressure

is comparable to the difference in blood pressure between individuals with high and low genetic risk of hypertension based on SHGR, which will be presented below.

The purpose of this review is to analyze the literature data on the assessment of SHGR AG.

Methodological approaches. The search for literary sources was carried out in the search engines PubMed, RSCI. Keywords and their combinations were used as search queries: "hypertension", "genetic risk score", "blood pressure", "genetics", "arterial hypertension", "genetic risk scale". The search depth was 13 years (in addition, earlier publications are included in the "Introduction" section). To date, a number of CVD risk scales have been developed, including hypertension. In the study.

The chance of having AH per one standard deviation (SD) of SHGR was increased by 23% (95% confidence interval (CI): 1.86-2.36), and in persons belonging to the upper decile of SHGR, the prevalence of AH was 29 vs 16% of the lower decile. This scale also demonstrated an association with the wall thickness of the left ventricle, stroke and coronary artery disease. However, according to the authors, the combination of these variants together explains 0.9% of the phenotypic variance of AD. Fava C, et al. (2013) [15] in a prospective study, which included >17 thousand a middle-aged man from Sweden, assessed how SHGR out of 29 GNP is associated with BP and the development of AG. The observation was carried out for 23 years. SHGR was associated with a higher blood pressure level both at the beginning of the study and in dynamics. The increase in SAD and diastolic blood pressure (DBP) by 1 SD SHGR was 1.0-1.3 mmHg and 0.6-0.7 mmHg, respectively. The difference in SAD between individuals from the upper and lower quartile was 2.6-3.5 mmHg, and the difference in DAD was 1.6-2.0 mmHg. The odds ratio (OR) for the presence of AH, regardless of the traditional FR, at the time of inclusion and in dynamics was 61 and 47% higher for persons of the upper quartile compared to persons from the lower quartile, respectively. In the linear regression model, the association of SHGR with a change in blood pressure is demonstrated. The relative contribution of SHGR to the presence of hypertension was lower than for obesity and initially high normal blood pressure, but at the same time comparable with a family history of hypertension and the presence of diabetes mellitus. A Finnish prospective study of SHGR AH, including 13 GNP, also demonstrated an association with AH, independent of the family history of this disease [16]. This study is interesting because the observation began in childhood, it included participants aged 3-18 years, the blood pressure level was assessed in dynamics after 3, 6, 21 and 27 years. For participants from the upper quintile, the OSH of hypertension development in adulthood was 1.82, regardless of the family history of early hypertension. In another study [17], it was studied how SHGR, including 32 GNP associated with the development of hypertension, allows predicting the development of CVD. The study included 32,669 people without coronary heart disease at the time of inclusion. The average follow-up period was 9.8 years. Separately for SAD and DAD, SHGRS (SHGRSAD and SHGRDAD) were developed, for which the relationship with the development of coronary

heart disease, stroke and CVD in general was demonstrated. The risk ratio (HR) for CHD was 1.25 (95% CI: 1.07-1.46) and 1.23 (95% CI: 1.05-1.43); HR for ischemic insoult – 1.24 (95% CI: 1.01-1.53) and 1.35 (95% CI: 1.09-1.66); OR for CVD in general — 1.23 (95% CI: 1.08-1.40) and 1.26 (95% CI: 1.11-1.44) for SHGRSAD and SHGRDAD, respectively. As part of the study of genetic factors of BP, including the analysis of 128272 GNP in 201529 individuals of European origin, 66 loci associated with BP were identified, of which 17 were identified for the first time [18]. SHGR AG was developed on the basis of 66 GNP, which explained 3.46 and 3.36% of the variance of SAD and DAD, respectively. SHGR also showed a significant association with damage to various target organs.

Based on 1 mmHg increase in blood pressure (based on the developed scales), the risk of coronary heart disease increased (OR 1,042 and 1,069 for SHGRSAD and SHGRDAD, respectively) and stroke (OR 1,058 and 1,089 for SHGRSAD and SHGRDAD, respectively).

It was demonstrated that the frequencies of alleles differed between ethnic groups. In addition, many GNPs had no significant association with the trait under study. Possible reasons for such differences include the authors: 1) the smaller size of non-European samples; 2) the difference in the non-equilibrium linkage of GNP (linkage disequilibrium) between ethnic groups, 3) the difference in allele frequencies, 4) the absence of a true association between GNP and a trait in some ethnic groups. The size of the GNP effect on both SAD and DAD coincided for European and South Asian samples for 45 out of 66 GNP, East Asian — for 36 out of 66 GNP and 42 out of 66 for African samples. The association of the SHGR value with the blood pressure level remained, but was weaker than for European samples. In the work of Warren HR, et al. (2017) [19], on the basis of 146 GNP associated with blood pressure indicators, a SHGR was developed to assess the likelihood of developing hypertension. The sample consisted of persons ›50 years old, the analysis was adjusted for gender. Participants corresponding to the upper quantile of SHGR had SAD at 9.3 mmHg. higher than the participants from the lower quantile of SHGR (95% CI: 6,9-11,7),

Despite the fact that family history is a good indicator of hereditary predisposition to the development of hypertension, this parameter cannot be considered sufficient to determine the genetic risk of this disease, since it is limited to a small number of relatives, is not always reliable or may be absent altogether. Family history of hypertension has an association with the risk of its development, but its absence, in turn, does not mean the opposite [20].

Conclusion. Given the fact that genetic risk is available for determination from birth and has not changed over time, its determination from a young age seems promising, since it can be implemented until the effect of environmental factors manifests itself. It seems promising to introduce into clinical practice the use of SHGR to determine the genetic predisposition to the development of hypertension, because it will make it possible to identify a risk group even at an early age, which will determine the need for intervention, adjust lifestyle, increase adherence to taking medications, and thereby weaken growth.

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