Predisposing genetic factors in cardiovascular diseases

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Cardiovascular disease (CVD) is the most common cause of morbidity and mortality in developed countries, with coronary heart disease (CHD) accounting for 40% of CVD deaths. Approximately 25,000 cases of myocardial infarction are diagnosed annually in the Czech Republic, 5 times more often in men, and hospital mortality is approximately 4-6%. The importance of CVD prevention follows from this, while knowledge of genetic predisposing factors can help timely and consistent prevention.

Ischemic heart disease is caused by atherosclerosis and involves a wide range of clinical manifestations, such as angina pectoris, myocardial infarction (MI) and sudden cardiac death. The familial occurrence of this disease shows a significant influence of genetic factors. Risk factors for CHD are divided into controllable and uncontrollable factors. We rank among the influenceable risk factors. arterial hypertension, dyslipidemia, degree of abdominal obesity, type 2 diabetes mellitus, smoking, eating habits, lack of physical activity and some psychosocial factors.

Uncontrollable risk factors are genetic predisposition, age, sex, metabolic syndrome and prenatal hypoxia. Heritability, the share of the genetic component in the development of cardiovascular diseases is estimated at 40% -60%. Today we know. Cardiovascular disease (including coronary heart disease) develops on the basis of the lifelong action of environmental factors in relation to genetic factors (our genome).

We distinguish CHD arising on a monogenic basis. It is diagnosed in a minority of individuals. Predisposition in these patients is due to inheritance of the mutation in one of the following genes: ST6GALNAC5, MEF2A, LRP6, the gene for LDL receptor, PCSK9, ApoB-100, LDLRAP1 (genes whose mutations cause high LDL cholesterol), and a gene whose mutation causes low HDL cholesterol - ABCA1 gene and genes whose mutations cause high levels of triacylglycerols, for example the ApoC-II gene.

In most patients, coronary heart disease develops on a polygenic basis. Risk genetic variants for coronary heart disease are very common, individual gene alleles occur in the population with a frequency of 2% to 91%. We each carry some risk variants in our genome. Those with a high genetic risk for coronary heart disease have inherited a greater number of risk variants. The relative increase in risk for one risk genetic variant is small, on average 18%. GWAS studies and association studies of candidate genes have revealed dozens of genes whose risk alleles are involved in the development of coronary heart disease. These are genes that are involved in the metabolism of cholesterol, triacylglycerols, blood clotting, hypertension, etc. A large number of risk variants for coronary heart disease are found in DNA sequences that do not encode proteins. These risk variants increase the risk of CHS by altering the regulation of gene expression.

At present in suspects individuals, a number of these risk alleles of genes, their knowledge enabling lifestyle modifications, are being investigated, however, comprehensive testing is not yet recommended.