Abstract

Familial hyperlipidemias are still a current cause of premature development of atherosclerotic cardiovascular disease (ASCVD). Heredity plays an important role in the development of these diseases. Genetic testing helps to specify a definite variant of a given disease and thus the degree of genetic family burden. Together with the clinical examination, it defines the exact diagnosis of the patient and reduces the risk of developing ASCVD in individual specialized care.

In the theses, we focused on biochemical and genetic differences and their risk factors for the development of ASCVD in long-term monitored patients with familial hypercholesterolemia (FH), in receptor-mediated FH and familial defect of apolipoprotein B-100 (FDB). Efficacy, safety, and tolerability of therapy were evaluated in a subgroup of FH patients with PCSK9i therapy. Furthermore, the polygenic genetic risk score (GRS) in patients with the *APOE2E2* genotype and its influence on the early detection of the development of familial dysbetalipoproteinemia (FD) were analyzed.

Receptor-mediated FH patients carry a mutation in *LDLR* while FDB patients have a prevalent mutation in *APOB*. LDL-C and TC levels are high in both groups, although levels are slightly higher in receptor-mediated FH patients. *APOE* genotype and risk factors such as diabetes mellitus or arterial hypertension also influence LDL-C levels and increase the risk of CVD. Research in biochemistry and genetics has contributed to the development of therapeutic options. Modern PCSK9i therapy has brought positive results in reducing LDL-C levels, and as it is well tolerated, effective, with few negative side effects, it is a beneficial therapy even for statin intolerants. Unweighted GRS is a suitable auxiliary predictor of the development of FD in patients with the *APOE2E2* genotype.

Further study of the genetic factors of FH will lead to an improvement in the prognosis of patients with this disorder, which we can document in our patients, when LDL-C levels decreased from 6,49 ± 1,92 mmol/l to 3,26 ± 1,57 mmol/l, i.e. by almost 50%. This is also the reason why we will continue studying this issue.