Summary

Coronary artery disease (CAD) is associated with many unfavorable consequences affecting both the condition of the individual and the entire society. Despite the knowledge of the classical CAD risk factors, the morbidity and mortality remains high. As a consequence, new, potentially modifiable factors that may play a role in the development of atherosclerosis and lead to CAD, like gut microbiome, are taken into consideration.

The microbiota is the endogenous microflora of the human body mostly, but not exclusively, inhabiting the digestive system. It has been shown that bacteria form an ecosystem of mutual dependencies with the host, influencing both the metabolism and the host's immune processes. This may lead to CAD development and become an important part of the pathogenetic process.

In the presented study, we examined the gut microbiome of 169 CAD patients and 166 people in the control group, matched in terms of age and sex to the CAD group. Both populations underwent a detailed health assessment, with particular emphasis on the cardiovascular system.

Purified genomic DNA of microorganisms living in the large intestine was isolated from the stool samples. Further analysis of the microbiome was based on bacterial composition determining based on the sequencing of the gene encoding the 16S rRNA by Next Generation Sequencing method. The gene encoding 16S rRNA, included in the smaller subunit (30S) of the prokaryotic ribosome, is considered to be the best phylogenetic tool due to conserved fragments that are characteristic for certain taxonomic groups and enable their identification. Among 4074 identified taxonomic units in the whole population, 1070 differed between study groups. The most common bacterial types were Firmicutes, Bacteroidetes, Proteobacteria, and Actinobacteria. Furthermore, a higher Firmicutes/Bacteroidetes ratio in the CAD group compared with the control was demonstrated.

Firmicutes/Bacteroidetes ratio, independently of age, sex, CAD status, LDL cholesterol concentration, and statins treatment, was related to altered phosphatidylcholine and sphingomyelin concentrations obtained in targeted metabolomics. Altered alpha-biodiversity and beta-biodiversity in the CAD group were observed. Moreover, a predicted functional analysis revealed some taxonomic units, metabolic pathways, and proteins that might be characteristic of the CAD patients' microbiome, such as increased expressions of 6-phospho-beta-glucosidase and protein-N(pi)-phosphohistidine-sugar phosphotransferase and decreased expressions of DNA topoisomerase, oxaloacetate decarboxylase, and beta-glucosidase.

In addition, careful analysis of the literature allowed identify potential relationships between the gut microbiota and modifiable (diet, physical activity, smoking, overweight and obesity, lipid profile) and non-modifiable cardiovascular risk factors (age, gender). The role of short-chain fatty acids has been presented as one of the important mechanisms of the influence of the microbiome on the host. A higher Firmicutes/Bacteroidetes ratio has been shown to be associated with particular components of the diet, selected cardiovascular risk factors and cardiovascular diseases.

Demonstration of differences in the composition of the CAD intestinal microbiome in relation to the control group, might allow the identification a potentially modifiable risk factor, which might allow undertaking specific diagnostic and therapeutic actions. This may, in the long run, contribute to the CAD morbidity and mortality reduction. In addition, identifying the functional potential of the gut microbiome will contribute to better understanding of the complex

interactions between microorganisms and their hosts. It should be emphasized that even a small decrease in the risk of complications of such a common disease as CAD, could results into significant economic and social cost reduction in the context of the functioning of the entire society.