

## Abstract

Current applied research of microRNA molecules is focused on the identification of their roles in the pathogenesis of various types of diseases, including cardiovascular (CV), with the assumption of their use as biomarkers or treatment targets. Cardiovascular diseases have a high incidence and prevalence in the population, are predominantly chronic, and are also a leading cause of hospitalization and death, and therefore represent a major burden on patients and the health system.

Many metabolic parameters are currently used in the diagnosis of cardiovascular diseases and cardiovascular risk assessment, mostly proteins and lipids, while parameters from the group of nucleic acids, whether in the form of mutations in DNA molecules, or various RNA molecules, are very limited so far. Despite the undeniable importance and contribution of metabolic biomarkers in the diagnosis and prognosis of cardiovascular diseases, these markers still do not allow effective identification of all patients at high risk, and therefore additional molecules are being sought that could contribute to the accuracy of this identification.

Finding other potential diagnostic and prognostic markers to contribute to the more precise CV risk assessment, and subsequently also to the more effective treatment of patients at high risk, is the topic of this dissertation. We focused on a group of microRNAs, short non-coding RNAs, involved in the post-transcriptional regulation of gene expression, influencing the expression of most protein-coding genes in humans. MicroRNAs are synthesized in cells, passively and actively released into the circulation, where they are relatively stable, and can be determined in both tissues and various body fluids, including blood. In addition, the expression levels of many microRNAs change in relation to the various pathological conditions or acute events, and these changes can be very dynamic.

MicroRNAs were isolated from tissues and plasma, and their expression levels were measured, using molecular biological methods, in order to set a diagnosis or improve its setting, or to improve prognosis estimation for particular cardiovascular diseases. In aortic tissue, microRNA expression levels were compared between tissues with and without aortic abdominal aneurysm (AAA). In acute myocardial infarction patients, plasma levels of selected miRs were determined, as well as in patients in secondary prevention of CV diseases, and in patients with obstructive sleep apnoea syndrome, where heart diseases are very common comorbidities.

In order to find microRNAs involved in the pathogenesis and progression of the abdominal aortic aneurysm, we identified a panel of miRs dysregulated in AAA tissue compared to healthy controls, in both small and large aneurysms. In the future, these microRNAs may help identify patients at risk for more dynamic disease progression, or increased risk of rupture. In patients with myocardial infarction, we identified miR-499 as the most promising biomarker of all the microRNAs we analysed, with the greatest potential to contribute to the high risk patients identification, having the highest annual risk of death. In the group of chronic patients after a CV event, we found that decreased miR-19a expression levels are associated with a higher risk of death, and therefore they may be used as a prognostic biomarker of mortality. We further identified miR-499 as a potential additional diagnostic biomarker in patients with obstructive sleep apnoea syndrome.

We succeeded to identify at least one miR as a potential diagnostic or prognostic marker for all studied diagnoses, and to discuss its involvement in pathological processes.