Abstract

Ischemic heart disease, most commonly in the form of myocardial infarction (MI), is the leading cause of heart failure (HF) in developed countries. Despite advances in the treatment of MI, the residual risk of cardiovascular events remains high after MI. HF is the most common cause of morbidity and mortality in patients after MI. Its development is associated with a threefold higher risk of mortality regardless of left ventricular ejection fraction.

The aim of our work was to determine the prognostic significance of the remote diagnosis of symptoms and signs of HF one month after discharge from the hospital. We found that the Kansas City Cardiomyopathy Questionnaire (KCCQ) can identify individuals at increased risk of death independently of other risk factors that influence prognosis after MI. This finding confirms the clinical importance of early diagnosis of HF after MI.

Because not all components of the KCCQ questionnaire are prognostically important in patients after MI, in further work we identified 3 questions from the KCCQ that best predict the risk of mortality after MI. These included the level of limitation in walking, the presence of lower extremity swelling, and the change in symptoms over the past 2 weeks. In the validation cohort, we identified additional clinical variables influencing mortality after MI. By combining clinical variables and symptoms and signs of HF, we created a new prognostic score – the PragueMi score. In the validation cohort, our PragueMi score had better discrimination, calibration and reclassification capabilities than the currently recommended GRACE (Global Registry of Acute Coronary Events) score.

As part of the search for new possible therapeutic targets, we analysed the relationship between iron deficiency and the risk of total mortality after MI. As there are currently no hard data-based criteria for iron deficiency (ID) after MI, we analysed the predictive value of various parameters of iron metabolism. Based on our analyses, we created a new ID criterion called PragueID criterion, which is based on serum iron level and soluble transferrin receptor concentration. PragueID was able to stratify mortality risk independently of other clinical variables. In further work, it will be necessary to clarify whether clinical decision-making and iron substitution based on the PragueID can improve the prognosis after MI.

In another work, we pointed out the association between the activity of the orexin system and the risk of mortality after MI. Homozygotes for the minor T allele in the rs7767652 locus, located in the regulatory region for orexin receptor 2 and reduces the transcription of this receptor, as well as patients with lower orexin A concentrations, had a higher risk of mortality.

In our work, we further demonstrated that the prevalence of systolic dysfunction in post-MI patients is high even today. Those patients whose left ventricular ejection fraction improved had a better prognosis compared with those whose left ventricular ejection fraction remained below 40%. Inflammatory response to MI, but also the severity of the coronary atherosclerosis and the development of atrial fibrillation were negatively associated with the improvement of systolic function after MI.

My dissertation points to the clinical importance of early remote diagnosis of symptoms and signs of heart failure after discharge from the hospital for MI. The PragueMi questionnaire created by us can select high-risk patients who could benefit from an earlier outpatient check-up and titration of the recommended pharmacotherapy. Furthermore, my work points to iron substitution and increasing the activity of the orexin system as possible new therapeutic interventions for patients with MI. However, randomized intervention studies will be necessary to confirm the clinical significance of these interventions