Objective of the project

Dilated cardiomyopathy (DCM) is a serious cardiac disease characterized with heart enlargement (dilatation) and impairment of systolic and diastolic function that ultimately leads to the development of chronic heart failure (HF). After coronary artery disease and hypertension, DCM is the third most common cause of HF but the number one indication for heart transplantation. Unlike other causes, DCM typically occurs in adolescence among young adults and thus, becomes a life-long disease. Fibrosis of extracellular matrix (ECM) is one of the hallmarks of DCM and is typically observed in one third to one half of all patients. Fibrosis significantly contributes to the progression of HF symptoms, functional impairment, and increases the risk of ventricular re-entrant arrhythmias leading to increased morbidity and mortality in DCM. Despite contemporary treatments in DCM and HF, there is little salutary effect on ECM fibrosis, which in fact frequently progresses.

The topic of fibrosis has been studied extensively and numerous mechanisms are relatively well described. Main effector cells are fibroblasts and miofibroblasts, also collagen synthesis pathways, the impact of adrenergic or renin-angiotensin-aldosterone (RAAS) systems as well as cytokines and growth hormones have been well characterized in fibrosis.

Precise diagnosis and staging of cardiac fibrosis are of paramount importance for the risk assessment and monitoring of disease progression. On the other hand, data of cardiac fibrosis course are scarce. Endomyocardial biopsy (EMB) and microscopic assessment of cardiac samples has long been considered the gold standard of fibrosis assessment. However, numerous limitations of EMB exists, including highly questionable nature of performing repeated biopsies. Magnetic resonance imaging (MRI) with novel parameters allow for accurate quantification of cardiac fibrosis. Certain blood molecules, so called biomarkers, can be used to estimate the dynamics of fibrosis process. In patients with DCM and HF there is increased risk of arrhythmias, including life-threatening ventricular arrhythmias. Cardiac fibrosis increases the risk of arrhythmias. Thus, it is important to better understand the progression of fibrosis and arrhythmic risk.

In patients with DCM at baseline, the following studies will be performed: echocardiography, cardiac magnetic resonance, 48-hour Holter monitoring and measurements of biomarkers of fibrosis. Biomarkers studies will be performed at 3, 6, 9 and 12-month. At 12-month MRI will be repeated. At 12- and 18-month echocardiography and 48-hour Holter will be repeated. The final telephone visit, including assessment of the occurrence of the combined clinical end-point will be performed at 24 months after recruitment.

Justification for choosing research topic

Cardiac fibrosis is a complex process that is regulated on multiple levels and is still a subject of ongoing research. At present there are no proven anti-fibrotic treatments. The project will broaden our understanding on the course of myocardial fibrosis in DCM. Thus, main aim of the project is to develop an algorithm, based on large amount of clinical, imaging and biomarkers data, that may help to predict the course of fibrosis in DCM. The relationships between changes in fibrosis and cardiac (structural, functional and electrical) remodeling will be investigated. Better understanding of the basis of fibrosis may pave the way towards the development of tailored, effective and safe anti-fibrotic therapies.