Relationship between dynamics of cardiac sympathetic innervation, assessed with 123I-meta-Iodobenzylguanidine (MIBG) single-photon emission computed tomography, left ventricular reverse remodelling and exercise capacity in dilated cardiomyopathy.

Heart failure (HF) is a world-wide problem with a prevalence of 1-2% in the general population. During HF the heart undergoes various multilevel adverse changes. The most common etiology of HF in younger population is dilated cardiomyopathy (DCM). Several features distinguish DCM from the rest of HF, including different mechanisms of cardiac pathology, a unique clinical course that encompasses poorly understood phenomena of left ventricular reverse remodelling (LVRR), fewer comorbidities and lower mortality rates.
The autonomic nervous system, comprised of para- and sympathetic nervous systems (PSNS, SNS), regulates the cardiovascular system. The SNS is associated with the *"fight and flight"* response, while the PSNS is responsible for the restorative effects. In HF the continuous adrenergic (SNS) stimulation results in adverse cardiac remodelling – unfavourable functional and morphological changes. To reverse these adverse changes the multilevel neurohormonal blockage is recommended, including SNS blockade by β-blockers (BB). The improvement of left ventricle function and morphology (LVRR process) during BB therapy were confirmed and widely-accepted only 2 decades ago. Further, after the introduction of BB therapy, the decrease of the adrenergic drive was reported. One of the most practical and feasible tools to study cardiac SNS is a single-photon emission computed tomography (SPECT) with ^{123}I-meta-Iodobenzylguanidine (MIBG). During HF development the altered SNS results in abnormal SPECT results (lower MIBG uptake and higher MIBG washout rate). The degree of myocardial MIBG uptake impairment was found to be associated with worse prognosis in HF and DCM. The explanation for this phenomena is unknown, but it is suggested to be associated with LVRR and SNS function normalisation during this process.

The study aims to analyse the relation between cardiac SNS function (by SPECT with MIBG), LVRR presence (in transthoracic echocardiography, TTE), exercise tolerance (in cardiopulmonary exercise test, CPX) and HF laboratory profile (NT-proBNP, troponin, CRP).

STUDY DESIGN
30 patients with early onset of DCM (< 6 months) and stable HF symptoms (NYHA I-III ≥ 2 weeks) will be included in the study. All patients underwent clinical examination, TTE, CPX and laboratory tests at baseline, 12- and 24-months follow-up. Moreover, the MIBG-SPECT will be performed at baseline and 12-month follow-up. According to baseline and 12-month TTE the LVRR presence will be established. Baseline and 12-months MIBG uptake will be compared between LVRR-present and -absent groups. The changes (kinetics) in MIBG uptake between baseline and 12-months follow-up will be calculated for both groups separately. The MIBG uptake's kinetics will be compared between LVRR-present and -absent groups. Moreover, between 12- and 24-months observation the LVRR maintenance in the LVRR-present groups and the late LVRR presence in the LVRR-absent group will be analysed.

EXPECTED IMPACT
The optimal medical therapy of HF includes among others neurohormonal blockage of the adrenergic system (BB), which undisputedly improve HF and DCM patients prognosis, but the physiological process underlying the mechanism of this improvement is unconfirmed. Therefore, by observing changes in SNS function during LVRR in clinical settings we will broaden the knowledge on the LVRR functional mechanism, and empower the effort made towards increasing its incidences. Moreover, the analysis of exercise capacity during LVRR in context of SNS function will enable us to decrease patients' HF symptoms and increase quality of life.
To change approach to HF therapies based on different cardiac adrenergic innervation, the novel, more independent and irrespective from observers, attitude towards MIBG scintigraphy is needed. Thus, the novel quantitative parameter will be introduced with standardize and unify results based on the computer analysis.