1) The objective of the project

The aim of the study is to evaluate the role of peripheral chemoreceptors in exercise intolerance in patients with heart failure with preserved ejection fraction (HFpEF). We plan to prove that peripheral chemoreceptors' sensitivity is augmented in aforementioned population and plays important role in provoking symptoms of exercise intolerance.

Peripheral chemoreceptors (PChRs) are structures located along main neck and thorax arteries. Their role is to maintain adequate oxygenation in bloodstream. The stimulation of PChRs activates some parts of the brain that makes breaths deeper and increases their frequency in order to restore optimal blood oxygenation. These structures have an excitatory effect on sympathetic system that accelerates pulse and elevates blood pressure.

In patients with heart failure with reduced ejection fraction there are some premises where oversensitivity of peripheral chemoreceptors leads to exacerbation of dyspnea and exercise intolerance. It is likely that similar mechanisms may be responsible for provoking symptoms in diastolic heart failure but so far it has not been proven.

2) Methods

The goal of the study is to enroll 50 patients with HFpEF. Apart from physical examination, filling in heart failure questionnaires, ECG, blood sample analysis, echocardiography, 6-minutes walking test, every patient will perform peripheral chemoreflexes tests: two times in the interval of a few days. Moreover, the maximal and submaximal exercise test on a bicycle will be performed with a special mask through which many ventilatory paraments may be analyzed.

The peripheral chemosensitivity includes acute (which acts in response to certain stimulus e.g. hypoxia) and tonic response that plays a significant role in resting condition without excitatory effect of any stimulus.

The assessment of peripheral chemosensitivity will be performed using transient hypoxia method. In this test patient is supposed to breathe air with reduced oxygen concentration that causes transient and short fall in oxygen saturation that stimulates minute ventilation.

The peripheral chemosensitivity is estimated based on minute ventilation graph with reference to the nadir of oxygen saturation while breathing gas with lower oxygen concentration.

The tonic peripheral chemoreceptors sensitivity will be assessed on unforced breathing with atmospheric air with placebo (has no influence on chemoreceptors) and a drug (dopamine) infusion which inhibits PChRs. The expected effect of dopamine infusion due to the PChRs blocking is the fall in minute ventilation. The tonic PChRs sensitivity is equated to the difference between median values of minute ventilation obtained during placebo infusion and dopamine infusion.

The results will be compared to those received from the control group (25 healthy volunteers).

3) Present reasons for choosing the research topic

The interest of the problem has emerged from the fact, that the treatment of HFpEF is challenging and unsuccessful. Finding evidence that these structures are crucial in the pathogenesis of heart failure symptoms would bring new therapeutic options in these patients. Particularly, that recent data present the positive effect of deactivation of PChRs in patients with heart failure with reduced ejection fraction and hypertension.