

## **Abstract**

The prognosis of heart failure with reduced ejection fraction remains poor. Neurohumoral activation, including increased cardiac sympathetic nerve activity, plays an important role in the pathogenesis as well as disease progression. Recently, several neuromodulation strategies have been proposed that aim to directly affect the residual autonomic imbalance. Spinal cord stimulation is one of the proposed methods.

In the clinical part of this project, we assessed the mid-term effect of spinal cord stimulation on cardiac sympathetic nerve activity and the acute effect on autonomic balance. In the total study population, we did not detect any changes in cardiac sympathetic nerve activity or heart rate variability. However, we observed that the patients with high baseline sympathetic nerve activity or low heart rate variability responded favourably to therapy, reflected in reduced cardiac sympathetic nerve activity and increased heart rate variability. Considering these results, we conducted an experimental study focused on the effect of acute severe heart failure on heart rate variability. In a porcine model of hypoxic myocardial dysfunction, we observed a significant reduction in heart rate variability in all parameters recorded.

Our results indicate that spinal cord stimulation may improve autonomic imbalance in heart failure patients with high cardiac sympathetic nerve activity or low heart rate variability, and that heart rate variability is markedly reduced in severe heart failure. Therefore, we can hypothesize that patients with severe heart failure and pronounced autonomic imbalance may profit from neuromodulation therapy.

**Keywords:** spinal cord stimulation, heart failure, sympathetic nervous system, heart rate variability