Introduction: Malignant ventricular arrhythmias (VAs) is common and confers a substantial risk of mortality and morbidity in patients with chronic heart failure (CHF). The autonomic nervous system is validated to play a significant role in the genesis and maintenance of VAs. Carotid baroreceptor stimulation (CBS) modulates the autonomic nervous system by sympathetic suppression as well as vagal enhancement. Our previous study found long-term moderate-level CBS (ML-CBS) that decreased blood pressure (BP) improved cardiac dysfunction and reduced cardiac fibrosis and apoptosis by inhibiting myocardia intracellular PKA signaling pathway in CHF canines. In addition, we found low-level CBS (LL-CBS) without BP reduction exhibited anti-atrial arrhythmic potential by inhibiting left stellate ganglion (LSG) activity in 6-hour rapid atrial pacing canines. In this study, we further investigated the effects of LL-CBS and ML-CBS on ventricular electrophysiological properties and ventricular vulnerability to fibrillation in CHF canines and its underlying mechanism.

Methods: Thirty-eight beagles were randomized into control (CON, n = 8), CHF (n=10), LL-CBS (n=10) and ML-CBS (n=10) groups. The CHF model was established by 6-week rapid right ventricular pacing (RVP), concomitant LL-CBS and ML-CBS were applied in the LL-CBS and ML-CBS group, respectively. After 6-week RVP, ventricular electrophysiological parameters, LSG neural activity and function were measured. Autonomic neural remodeling in LSG and left ventricle (LV), ionic remodeling in LV were detected.

Result: After 6-week RVP, compared with CHF group, both LL-CBS and ML-CBS decreased spatial dispersion of action potential duration (APD), suppressed APD alternants, reduced ventricular fibrillation (VF) inducibility, as well as inhibited enhanced LSG neural discharge and function. Only ML-CBS significantly inhibited ventricular effective refractory period and APD prolongation and increased VF threshold. Moreover, ML-CBS inhibited the increase in growth associated protein-43 and tyrosine hydroxylase-positive nerve fiber densities in LV, increased acetylcholinesterase protein expression in LSG, and decreased nerve growth factor protein expression in LSG and LV. Chronic RVP resulted in remarkable reduction in proteins expression encoding for both potassium and L-type calcium currents, these changes are partly amended by ML-CBS and LL-CBS.

Conclusion: CBS suppressed VF in CHF canines, potentially by modulating autonomic nerve and ion channels. And the effects of ML-CBS on ventricular electrophysiological properties, autonomic remodeling and ionic remodeling were superior to that of LL-CBS.