PO 043

Endothelin-1 enhances transmural heterogeneities in healthy porcine ventricular myocardium

Ms Alba Pérez-Martínez[1,2], PhD Esther Pueyo[1,2,3], PhD Aida Oliván-Viguera[1,2,3]
[1] *Biomedical Signal Interpretation and Computational Simulation (BSICoS), Engineering Research Institute of Aragon (I3A), University of Zaragoza, Zaragoza, España,* [2]*Institute for Health Research Aragón, IIS Aragón, Zaragoza, España,* [3]*Biomedical Research Networking Center in Bioengineering, Biomaterials and Biomedicine (CIBER-BBN), Zaragoza, España*

Background: Endothelin-1 (ET-1) is an autocrine/paracrine factor secreted by endothelial cells, cardiomyocytes and fibroblasts. In the heart, ET-1 is associated with physiological and pathophysiological processes, such as oxidative stress, apoptosis regulation and ventricular remodeling associated with heart failure and ischemic cardiomyopathy. ET-1 has been shown to modulate calcium and potassium currents and to contribute to arrhythmogenesis and sudden cardiac death.
Aims: To characterize the role of ET-1 in cardiac electrophysiology across ventricular regions from base to apex and from endocardium to epicardium in healthy pigs.
Methods: Domestic pigs (85-120 kg, n=4) were cardioplegically arrested under deep anesthesia and sacrificed. Transmural ventricular blocks of 1 cm2 area were taken from six ventricular regions: A) at the base, close to the left anterior descending (LAD) artery; B) at the base, close to the left circumflex (LCx) artery; C) at the center, near the LAD; D) at the center, near the LCx; E) at the apex; and F) at the center, in the posterior wall. 350 µm-thick ventricular slices were produced from the subepicardium, mid-myocardium and subendocardium of each region. The slices were optically mapped and Action Potential Duration (APD) was measured at 80% repolarization while pacing at 1 Hz in the absence and presence of 100 nM ET-1. The notation n/N indicates n slices from N pigs.
Results: ET-1 prolonged APD in all ventricular regions, with a mean prolongation of 18% (n/N=57/4). APD prolongation in the subendocardium (30%, n/N=13/4) was remarkably larger than in the mid-myocardium (14%, n/N=27/4) and subepicardium (14%, n/N=17/4), with the increased prolongation in the subendocardium being consistent across all six tested regions. No significant apex-to-base differences were observed.
Conclusions: ET-1 induces strong APD prolongation in pig myocardium, with enhanced responses in the subendocardium. Transmural heterogeneities in response to ET-1 might play a role in arrhythmia vulnerability.