

Modelling Effect of Heart Failure on The Electrical Activity of Sheep Atria

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Abstract

Heart failure (HF) is associated with cardiac arrhythmias, which are one of the most life-threatening conditions of cardiac diseases. HF impairs cardiac electromechanics that causes dysfunction of cardiac muscle contraction leading to increased risks of morbidity and mortality. Previous studies have revealed that HF causes alteration to the electrophysiological and structural properties of the atria.

The aim of this study was to investigate the effects of HF-induced remodelling on ion channels properties and the intracellular Ca^{2+} handling on the dynamical behaviours of electrical excitation waves in sheep atria.

The biophysically detailed model of sheep atrial action potentials developed by Butters et al. was modified to incorporate experimental data of HF-induced remodelling on ion channels (downregulation of the L-type calcium current (I_{CaL}), the slow delayed rectifier potassium current (I_{Ks}), and the transient outward potassium current (I_{to}), and upregulation of the inward rectifier potassium current (I_{K1}) and the $Na^+ - Ca^{2+}$ exchange current (I_{NaCa})) and Ca^{2+} handling. The developed atrial cell models in HF were then incorporated into the 3D anatomical sheep atria model in our previous study. The 3D model considered both electrical heterogeneity and tissue anisotropy.

At the cellular level, HF shortened the action potential duration at 90% of repolarisation (APD_{90}) from 349.5 ms in control to 270 ms in HF. At 3D, re-entrant excitation waves were initiated by applied a premature stimuli in the pulmonary veins (PVs) sleeves region. In control condition, the initiated re-entrant excitation waves self-terminated and had a lifespan of 4.4 sec. However, in HF, the initiated re-entrant excitation waves sustained through the whole period of simulation 5 sec.

Such sustained re-entrant excitation waves were attributable to the abbreviated APD_{90} , leading to a decreased wavelength and conduction velocity of excitation wave. This study provides mechanistic insights into the understanding of pro-arrhythmic effects of HF-induced remodelling on ion channels and Ca^{2+} handling.