Modelling the Effects of Hypertension on Ventricle Cells of Human Heart

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Introduction: Systemic hypertension (HP) is one of the key risk factors for evolving cardiac hypertrophy and heart failure (HF). Previous studies have shown that cardiac hypertrophy is associated with altered excitation-contraction (E-C) coupling and enhanced myocardial contraction, whilst HF is associated with diminished contractility. However, the causative cellular and molecular mechanisms linking hypertension to HF are still unclear.

Aims: This study aimed to investigate the functional impact of hypertension on the cardiac mechanical dynamics and the contracting mechanisms of the left ventricular myocytes of human heart by using a multi-cellular two-dimensional (2D) model of the ventricular tissue in the HP condition.

Methods: An electromechanical model of human ventricular cell model (previously developed by our group) has been modified by incorporating available experimental data from rat ventricular cells under Sham (control) and HP conditions. Hypertrophy was modeled by incorporating experimental data of changes in sodium channel current, I_{Na}, the outward transient potassium channel current, I_{to}, the sodium-calcium exchanger current, I_{NaCa}, cell size and myofilament responses to Ca^{2+} in the cardiac cell.

Results: Simulations showed that HP produced: 1) prolongation of the action potential duration at 90% repolarization (APD_{90}) by approximately 4.7%; 2) an increase of the intracellular calcium concentration ($[Ca^{2+}]_i$) by 36%; 3) no marked change in the sarcomere length or the contractile force at the cellular level; 4) but in the 2D tissue level, an increased tissue's vulnerability for initiation and maintenance of re-entrant excitation waves.

Conclusion: Simulation results at the cellular level were consistent with experimental data, validating the HP model development. At the tissue level, simulation results indicated the pro-arrhythmic effects of HP, providing mechanistic insights into understanding the increased risk of ventricular fibrillation in hypertensive patients.