Interplay of Potassium Channels in Modulating the Action Potential of Human Ventricular Myocytes

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Potassium ion channels are key determinants of cardiac action potential (AP) activity. Their interplay in modulating the AP of human left ventricle has not been well characterized.

In the present study, our newly developed allosteric conformation model for rapid delayed rectifier (IKr) was incorporated into the ten Tusscher model for human ventricular tissue. The transmural densities of IKr, the slow delayed rectifier (IKs) and the transient outward channel (Ito) were refined based on the variable expression of underlying protein subunits. The interdependence of these channels were investigated by simulated channel block.

With an IKr density ratio of about 0.55:0.83:1 in epicardial (Epi),mid-myocardial(M) and endocardial (Endo) cells, a maximum conductance of 0.00792 nS/pF for IKr, 0.1778 nS/pF for IKs and 0.209 nS/pF for Ito, the modified model was able to reproduce an action potential duration (APD) of 311 ms in epicardial, 342 ms in M and 296 ms in endocardial cells at 1 Hz pacing. A frequency change from 1 Hz to 0.5 Hz resulted in an Epi APD difference of 20.27 ms, an Endo APD difference of 18.64 ms and an M APD difference of 31.92 ms. Blocking IKs or IKr in M cells showed that APD increased with the downregulation of Ito. Block of IKr led to a prolongation of APD90 by 9% in Epi, 23% in M and 15% in Endo cells, whereas block of IKs caused a prolongation of APD90 by 27% in Epi, 7% in M and 21% in Endo cells, respectively.

The modified ventricular model yielded the density distribution of potassium channels closer to the physiological ranges compared with that given by the previous model. The results about the response to individual channel blocks and the improved APD rate adaptation provided a basis for understanding abormal ventricular repolarization.