Electrical restitution properties of rabbit atrial tissue

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Atrial fibrillation (AF) is the most common form of arrhythmia in the clinic. The heterogeneity in action potential (AP) morphology and adaptation to pacing rates (electrical restitution) are thought to contribute to arrhythmogenesis. It is important to characterize the response of various cell types to pacing at very high rates which mimic conditions occurring during AF or tachycardia.

Intracellular APs of right atrial (n=12 cells), left atrial (n=14 cells) and pulmonary vein (n=6 cells) tissue-intact myocytes were recorded in response to pacing at various frequencies using *in vitro* intact rabbit tissue preparations.

The electrical restitution curves of various AP morphology parameters of each tissue-intact myocyte type were reconstructed and compared. There were significant differences in the AP morphology between different myocyte types. However there were no major differences in their restitution properties. All tissue-intact myocyte types displayed AP duration and amplitude alternans over a wide range of pacing frequencies. The myocytes also differed in the frequency at which 1-1 response to electrical stimulation was lost.

The restitution curves of right atrial, left atrial and pulmonary vein tissue-intact myocytes found in this study agree with the general observation, that there is a decrease in action potential duration at 90% of repolarization (APD90) or APD50 with increased pacing frequency in cardiac tissue. In addition, the analysis suggests that intact myocytes, regardless of their type, show a decrease in AP amplitude with increased pacing frequency. This appears due to a combination of a decrease in maximum diastolic membrane potential (the cell becoming more depolarized) and a decrease in the AP peak. There was also a decrease in the maximum upstroke velocity and an increase in APD5. That is, with an increase in pacing frequency APs became shorter and their phase 1 spike disappeared, giving way to a smooth transition from depolarization to repolarization.

In summary, this study suggests that there are some inter-regional variabilities in the AP morphology at various pacing frequencies under controlled *in vitro* conditions. Further experiments are required to quantify the significance of inter-regional variability in electrical restitution properties. This information will be used in the development of ionic models that can reproduce responses to rapid pacing protocols for the realistic modelling of AF.