Pharmacological Prevention of Paroxysmal Fibrillatory Episodes in 2D Atria Considering Atrial Dominant Frequency

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The suboptimal success of antiarrhythmic drugs in preventing episodes of paroxysmal Atrial Fibrillation (pAF) could potentially be addressed by considering how intersubject variability influences the response to the pharmacological treatment choice. This study investigates the impact of the AF dominant frequency (DF) during medication-free periods on the efficacy of two drugs (flecainide and vernakalant) in preventing AF episodes.

Paroxysmal atrial electrophysiology was simulated on a 2D tissue using a modified version of the Courtemanche human atrial model. Individual variations of ±30% and ±40% were applied to 11 parameters related to electrophysiological variability to build a population. For each profile, the width of the vulnerable window (VW_{width}) was computed using the S1-S2 protocol in the absence and presence of flecainide and vernakalant. Moreover, the DF was computed on simulations without drugs and the low frequencies (1^{st} percentile) and high frequencies (3^{rd} percentile) subgroups were defined.

Our results show that intersubject variability significantly influenced the drug-free DF and the performance of flecainide and vernakalant. Both drugs were effective at low frequencies, although vernakalant exhibited greater efficacy at reducing VW_{width} (-83±35%) compared to flecainide (-29±39%). At high frequencies, the drugs differed significantly in efficacy such that vernakalant showed a better reduction in VW_{width} (-46±39%), while flecainide caused slight increments (-5±30%). These significant differences between flecainide and vernakalant may be linked to the higher significant increase in the APD_{90} and the ERP observed when applying vernakalant, along with a stronger reduction of conduction velocity under flecainide application.

These findings suggest that the effects of flecainide and vernakalant on the prevention of pAF episodes may be affected by the drug-free DF and that vernakalant may be more effective in reducing the VW_{width} compared to flecainide, especially at high DF. This could help to improve the personalization of pharmacological strategies in pAF patients.