

Drug Dependent Circadian Variations in AV-nodal Properties During Atrial Fibrillation

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Background: The heart rate during atrial fibrillation (AF) is highly dependent on the conduction properties of the atrioventricular (AV) node. These properties can be affected using rate control drugs, mainly β -blockers or calcium channel blockers, often chosen empirically. Thus, characterization of drug-dependent differences in AV node function could contribute to optimized personalized treatment of AF.

Methods: We have created a mathematical network model of the AV node, divided into a fast pathway (FP) and a slow pathway (SP), with model parameters describing its refractory period (R) and conduction delay (D). Continuous and computationally efficient estimation of the model parameters from 24-hour ambulatory ECGs from patients with permanent AF ($n=60$) was achieved using a problem-specific genetic algorithm. Circadian variations in the resulting model parameter trends were quantified using cosinor analysis, and differences between treatment with β -blockers and calcium blockers – both for the individuals and the whole population – were assessed using a linear-mixed effect approach.

Results: The estimated model parameter trends from one patient under the influence of verapamil are shown in Figure 1, where the refractory period for the two pathways as well as the conduction delay in the SP increases during nighttime. Moreover, the mixed-effects analysis indicated increased refractoriness relative to baseline for all drugs in both pathways. For the β -blockers, an additional decrease in circadian variation for parameters representing conduction delay was observed. This indicates that the two drug types have quantifiable differences in their effects on AV-nodal conduction properties.

Conclusion: The proposed methodology enables analysis of circadian variation in AV node conduction delay and refractoriness from 24h ambulatory ECG, which can be used to monitor and possibly predict the effect of rate control drugs.

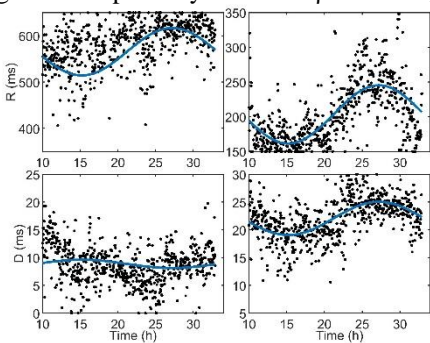


Figure 1: Estimated model parameters (black) and fitted cosines (blue) quantifying the refractory period (top) and conduction delay (bottom) in the FP (left) and the SP (right), respectively.