Mechanical Consequences of Electrical Remodeling due to Persistent Atrial Fibrillation: a Cellular Level Sensitivity Analysis

Jorge Sánchez[1,2], Axel Loewe[1]

[1] Institute of Biomedical Engineering, Karlsruhe Institute of Technology (KIT), Karlsruhe, Germany
[2] ITACA Institute, Universitat Politècnica de València, Valencia, Spain

Introduction: During atrial fibrillation (AF), the tissue undergoes electrical remodeling that alters myocyte electrophysiology. These changes in electrophysiology affect the contraction of the cells as well. While electrical remodeling has been characterized extensively, tension development data during AF are scarce.

Methods: We used the mathematical model of a human cardiac myocyte proposed by Skybsbye et al. coupled with the tension model proposed by Land et al. In this study, we systematically vary electrophysiological parameters from their baseline value toward atrial fibrillation remodeling. We analyzed action potential duration, peak intracellular calcium concentration, and maximum tension from single-cell electro-mechanical simulations and compared them to values reported from in vitro experiments.

Results: A total of 280 model variants were studied, of which 94 models reproduced the experimentally reported reduction of action potential duration. 11 models reproduced the reduction of the peak calcium concentration, and 4 models reproduced the reduction of peak tension observed in patients with atrial fibrillation. For the action potential duration variation, I_{K1}, I_{sus}, I_{to}, and I_{CaL} were the currents that were most sensitive. However, for tension development, the L-type Ca^{2+} channel played the biggest role. When I_{CaL} was reduced to between 75% and 81%, the action potential duration and the peak calcium concentration were in the range of the reported experimental data. As reported in experimental data, these model variants also yielded a maximum tension development reduction of around 75%.

Conclusion: Electrical remodeling due to AF has a marked impact on tension development, which is mainly mediated through reduced L-type Ca^{2+} current.