Reduced Conduction Reserve in the Diabetic Rat Heart: Insights from Experimental Observations and Computer Simulations

Anders Nygren[1,2], Haisam Ghaly[1], Gary Kargacin[3], Yyakhin Shimoni[3]
[1]*Department of Electrical and Computer Engineering – University of Calgary*
[2]*Centre for Bioengineering Research and Education – University of Calgary*
[3]*Department of Physiology and Biophysics - University of Calgary*

Conduction velocity is dependent on two main factors: intercellular electrical coupling and cellular electrical excitability. There is significant redundancy, "conduction reserve", in these parameters such that significant reduction in the conduction velocity of the action potential requires either a large change in one of these parameters or combined changes in both. We have used optical mapping to measure conduction velocity in hearts from streptozotocin-induced diabetic rats. Our results show little change in baseline conduction velocity in diabetic hearts compared to controls. However, both the gap junction uncoupler heptanol (0.5-1 mM), and elevated potassium (9 mM) produced a significantly greater reduction of conduction velocity in diabetic hearts than in controls. Immunofluorescent labeling of connexin-43 showed significant gap junction reorganization (lateralization) in diabetic hearts, which we hypothesize results in reduced intercellular coupling. To gain a better understanding of these effects, a rat ventricle myocyte model was used to simulate propagation along a strand of cells. Simulations were performed to assess the effect of reduction of intercellular conductance on the conduction velocity. Consistent with our experimental results, the relationship between conduction velocity and intercellular coupling became steeper with decreasing coupling, such that conduction velocity became increasingly sensitive to further uncoupling.