M-cell Heterogeneity Influence in Arrhythmic Pattern Formation in Sub-Epicardial Regional Ischemia: A Simulation Study

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Ventricular arrhythmias and myocardial ischemia are inseparable. The occurrence of lethal arrhythmia was related with myocardial injury, alterations of ionic conductance and metabolite concentrations. Ischemia altered in differential form the wall heterogeneity, the epicardium and M cell is more affected that endocardium. In this computational study, we calculate the vulnerability of reentry during different stages of regional sub-epicardial ischemia in dissimilar islands configurations of M cell intro the cardiac wall (Antzelevitchs Hypothesis). For this purpose, a modified version of the Luo-Rudy model (2000) was used to simulate cardiac action potentials. The main components of ischemia (hypoxia, acidosis and hyperkalemia) were considered in the model. The tissue comprises 150x300 cells, which include different islands of M cells up to 55% tissue area, 20% for epicardial cells and the rest of endocardial zone. An S1-S1 stimulation protocol was used, and the vulnerable window (VW) for re-entry was quantified for different degrees of acute ischemia. We show that re-entrant pattern arise in the tissue after an extrastimulus is delivered. The wavefront invade virtual tissue through the epicardial zone. The core of re-entrant front remains within the central ischemic zone. The value of the VW, measured as the window of coupling intervals which elicit re-entry, is dependent on the degree of ischemia and the distribution of M cell clusters. Under conditions which mimiqued the first 8.0 minutes of ischemia, VW=5 milliseconds (ms). The VW reached 10 ms the 8.25 minute, increasing to 18 ms at the 8.5 minute, and further to 28 ms in t=8.75 minutes, this values of VW are means in different distributions of M cell. The VW abruptly decreases to zero in the ninth minute. In conclusion, the model predicts that the VW for re-entry has a logistic behaviour during sub-epicardial ischemia, with re-entry paths comprising midmyocardial islands of tissue.