Mechano-Electrical Feedback during Cardiac Resynchronization Therapy?

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Cardiac Resynchronization Therapy (CRT) has emerged as an important therapy to improve pump function in patients with left bundle branch block (LBBB). Electrical excitation of the ventricles is synchronized by simultaneously pacing both ventricles. It is known that long-term asynchronous activation leads to a form of electrical remodeling, referred to as T-wave memory. T-wave memory is known to occur after a period of ventricular pacing, but its role during CRT is unclear. Evidence is growing that T-wave memory is induced by altered mechanical load, and thus is a form of mechano-electrical feedback (MEF). We hypothesize that this kind of MEF leads to local changes in the expression of L-type calcium channels, aiming at (partial) correction of local workload in the asynchronous ventricle, but also affecting local action potential duration (APD). The aim of the present simulation study was to investigate the effects of MEF during LBBB and CRT using a multi-scale computer model. The model described cellular electrophysiology and calcium handling as well as cardiac mechanics and hemodynamics. Ventricular electromechanics was represented by a single cardiac fiber, while physiological pressure-volume loops were obtained by simulating the systemic circulation. LBBB was simulated by stimulating the fiber at one end (activation time 108 ms) and CRT by simultaneous stimulation at both ends (activation time 54 ms). During chronic LBBB, MEF lead to a reduction in local differences in external work as well as in dispersion of repolarization. During acute CRT, systolic function was acutely increased as was dispersion of repolarization. As a consequence diastolic function (reflected by E/A-ratio) was reduced. With chronic CRT, dispersion of repolarization decreased and diastolic function improved. We conclude that MEF may lead to an increase in dispersion of repolarization during the early phase of CRT, which may lead to impaired diastolic function and to ventricular arrhythmia.