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Mechanical-Energetic Coupling in Cardiac Contraction and Heart Failure.

The energetic state of the myocardium is abnormal in decompensated heart failure: phosphate metabolite concentrations are altered and the ATP hydrolysis potential is diminished compared to normal healthy conditions. Although this metabolic dysfunction has been characterized in both patients and animal models, the potential functional consequences of the observed changes in energetic state on mechanical function are not known. We have conducted a series of modeling and experimental studies aimed at quantifying mechanical/energetic coupling in the heart, determining if/how energetic dysfunction contributes to mechanical failure, and testing the following predictions of computer simulations: (1.) Changes in phosphate metabolite concentrations (ATP, ADP, and Pi) that are observed to occur in decompensated cardiac hypertrophy impair force/tension development the heart through a direct effect on myofilament cross-bridge cycle kinetics; and (2.) The resulting impairment in wall tension development leads to systolic dysfunction. This talk will introduce the theoretical/computational basis of mechano-energetic coupling in cardiac contraction, describe our hypothesis on mechano-energetic dysfunction in heart failure, and present experimental tests of our theoretical model predictions. (Received September 20, 2016)