IMPAIRED SARCOLEMMA CALCIUM EXTRUSION RESERVE AS A MAJOR CAUSE FOR INCOMPLETE RELAXATION AND TACHYCARDIA-INDUCED CONTRACTURES IN MYOCARDIUM FROM PATIENTS WITH CONCENTRIC LEFT VENTRICULAR HYPERTROPHY

ACC Oral Contributions
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Authors: Don E. Selby, Martin M. LeWinter, Markus Meyer, University of Vermont College of Medicine, Burlington, VT

Background: Concentric left ventricular hypertrophy (LVH) is known to cause diastolic dysfunction and is present in most patients with heart failure with normal ejection fraction. Tachycardia can induce heart failure symptoms in these patients. To elucidate the effects of tachycardia on myocardial contractility and relaxation we evaluated the effects of increasing pacing rates in myocardial strip preparations from patients with and without LVH.

Methods: LV biopsies were obtained from 14 patients during coronary bypass surgery. All patients had a normal ejection fraction. Myocardial strip preparations were electrically paced at rates from 60/min to 180/min. Calcium transporting systems were examined by post-rest decay (PRD), rapid cooling contractures (RCCs), complete pharmacological sarcoplasmic reticulum inhibition (SRi) and by quantitative PCR.

Results: Seven preparations displayed progressively worsening incomplete relaxation at increasing pacing rates (p<0.01). This was absent in the remaining seven preparations. Analysis of the clinical data revealed that incomplete relaxation was present in biopsies from all patients with LVH (p<0.01). Additional functional analyses suggest that incomplete relaxation is associated with disproportionately elevated cellular calcium loads as demonstrated by RCCs (p<0.01) and PRD (p<0.05). Our SRi experiments suggest an impaired sarcolemmal calcium extrusion reserve is primarily responsible for incomplete relaxation and tachycardia induced contractures (p<0.05). Interestingly, we found 2 genes involved in the maintenance of sodium across the plasma membrane to be significantly downregulated in patients with LVH. These genes encoded the Na-K ATPase β2 and cardiac sodium channel β1.

Conclusions: Incomplete relaxation that lead to tachycardia-induced contractures were found in isolated myocardium from patients with concentric LVH. We also observed a disproportionate increase in cellular calcium load at high rates which appears to be due to a lack of sarcolemmal calcium extrusion reserve. These observations may play a central role in the reduced exercise tolerance and tachycardia induced heart failure symptoms in patients with LVH.