**IMPAIRED ENERGETICS AND HEART FAILURE: RATES OF ADENOSINE TRIPHOSPHATE TRANSFER THROUGH CREATINE KINASE PREDICT CLINICAL HEART FAILURE EVENTS AND DEATH**

**Background:** Morbidity and mortality from heart failure (HF) are high, and current risk stratification approaches for predicting HF progression are imperfect. Although ATP is required for normal cardiac contraction and abnormalities in energy metabolism have been observed in experimental and clinical HF, the prognostic value of abnormalities in the rate of ATP production through creatine kinase (CK), the major myocardial energy reserve, in human HF has not been investigated.

**Methods:** 58 HF patients with non-ischemic cardiomyopathy underwent 31P magnetic resonance spectroscopy (MRS) to quantify cardiac high-energy phosphates and the rate of ATP synthesis through CK (CK flux) and were prospectively followed for 4.6±2 years for HF related events including all-cause and cardiac death, hospitalization for heart failure, cardiac transplantation and ventricular-assist device placement. Multiple event analysis (MEA) was performed for the HF composite.

**Results:** HF patients (mean age 48.7±11.2 years (mean±SD), women 32.8%) had a mean LVEF 25.8±15.7% and NYHA class 2.2±0.8. Only 5% of patients were lost to follow-up and all-cause and cardiovascular mortalities were 33% and 24%, respectively. Mean myocardial CK flux was significantly lower in patients who experienced cardiac death (1.18±0.68 μmol/g wet wt/sec) than in those that did not (2.0 ±0.97 μmol/g wet wt/sec, p<0.01). MEA identified four independent predictors of HF events: NYHA class≥3 (HR 2.92, p<0.001), African American race (HR 3.60, p<0.001), and myocardial CK flux (HR 0.65, p<0.01). For each 1 μmol/g/sec increase in ATP flux through CK, risk of HF related composite outcomes decreased by 39%.

**Conclusion:** Reduced rates of ATP synthesis through myocardial CK, the primary cardiac energy reserve reaction, are an independent predictor of HF outcomes in patients with mild-to-moderate HF. These findings suggest that non-invasive 31P MRS may complement HF risk stratification and that reduced CK flux is a potential HF treatment target.