ABNORMAL MYOCARDIAL ENERGETICS IN CHRONIC HIBERNATING MYOCARDIUM AT HIGH CARDIAC WORK LOAD

ACC Poster Contributions
Georgia World Congress Center, Hall B5
Sunday, March 14, 2010, 3:30 p.m.-4:30 p.m.

Session Title: Myocardial Energetics and Protection
Abstract Category: Myocardial Ischemia/Infarction--Basic
Presentation Number: 1104-302

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Background: We previously reported that the myocardial energetic state, as defined by PCr/ATP, was preserved at baseline in a swine model of chronic myocardial ischemia with a mild reduction of myocardial blood flow (MBF) 10 weeks after placement of an external constrictor on the LAD. The follow-up period in this study was limited by the large size of the Yorkshire pigs which limited their placement in the magnetic bore for the Magnetic Resonance Spectroscopy (MRS) study. It remains to be seen whether this stable energetic state is maintained at a longer term follow-up.

Methods: Hibernating Myocardium (HB) was created in mini-pigs (n=7) by the placement of an external constrictor (1.75 mm i.d) on the LAD after thoracotomy. Ventricular function was assessed with MRI at regular intervals until 6 months. At 6 months, myocardial energetic state in the LAD region (HB) was assessed by 31P-MRS and myocardial oxygenation was examined from the deoxymyoglobin signal using 1H MRS during baseline (BL), coronary vasodilation with adenosine (AD) and increased work-load with dopamine and dobutamine (DD). MBF was measured with radiolabeled microspheres.

Results: At BL, wall thickening fraction was significantly lower in the HB as compared to remote region (34.4±9.4 vs 50.1±10.7, p=0.006). This was associated with a decreased MBF in the HB as compared to remote region (0.73±0.08 ml/min.g vs 0.97±0.07 ml/min.g, p=0.03). The HB PCr/ATP ratio at BL was normal. AD caused a similar level of increase in MBF in the HB and remote region. DD resulted in a significant increase in RPP, which caused a 2 fold increase in MBF in the HB and a 3 fold increase in the remote region. The systolic thickening fraction increased with DD, which is significantly higher in the remote region than HB (p<0.05). The high cardiac work load (HWL) was associated with a significant reduction in the HB PCr/ATP ratio (p<0.02). The ATP production rate via Creatine Kinase was also reduced by 20.4±0.12% during DD.

Conclusions: Thus, HB has stable baseline myocardial energetic despite reduction in MBF and regional LV function. More importantly, HB has a reduced contractile reserve, which is accompanied by a reduced myocardial energetic state at HWL.