Relation of myocardial oxygen consumption and function to high energy phosphate utilization during graded hypoxia and reoxygenation in sheep in vivo.

Portman MA, Standaert TA, Ning XH.

Department of Pediatrics, University of Washington, Seattle 98195, USA.

This study investigates the relation between myocardial oxygen consumption (MVO2), function, and high energy phosphates during severe hypoxia and reoxygenation in sheep in vivo. Graded hypoxia was performed in open-chested sheep to adjust PO2 to values where rapid depletion of energy stores occurred. Highly time-resolved 31P nuclear magnetic resonance spectroscopy enabled monitoring of myocardial phosphates throughout hypoxia and recovery with simultaneous MVO2 measurement. Sheep undergoing graded hypoxia (n = 5) with an arterial PO2 nadir of 13.4 +/- 0.5 mmHg, demonstrated maintained rates of oxygen consumption with large changes in coronary flow as phosphocreatine (PCr) decreased within 4 min to 40 +/- 7% of baseline. ATP utilization rate increased simultaneously 59 +/- 20%. Recovery was accompanied by marked increases in MVO2 from 2.0 +/- 0.5 to 7.2 +/- 1.9 mumol/g per min, while PCr recovery rate was 4.3 +/- 0.6 mumol/g per min. ATP decreased to 75 +/- 6% of baseline during severe hypoxia and did not recover. Sheep (n = 5) which underwent moderate hypoxia (PO2 maintained 25-35 mmHg for 10 min) did not demonstrate change in PCr or ATP. Functional and work assessment (n = 4) revealed that cardiac power increased during the graded hypoxia and was maintained through early reoxygenation. These studies show that (a) MVO2 does not decrease during oxygen deprivation in vivo despite marked and rapid decreases in high energy phosphates; (b) contractile function during hypoxia in vivo does not decrease during periods of PCr depletion and intracellular phosphate accumulation, and this may be related to marked increases in circulating catecholamines during global hypoxia. The measured creatine rephosphorylation rate is 34 +/- 11% of predicted ($P < 0.01$) calculated from reoxygenation parameters, which indicates that some mitochondrial respiratory uncoupling also occurs during the rephosphorylation period.