

Lewandowski E, X Yu, K LaNoue, L White, C Doumen, M O'Donnell. Altered metabolic exchange between subcellular compartments in intact postischemic rabbit hearts. *Circ Res* 1997;81:165-175.

To examine metabolic regulation in postischemic hearts, we examined oxidative recycling of ^{13}C within the glutamate pool (GLU) of intact rabbit hearts. Isolated hearts oxidized 2.5 mmol/L [2- ^{13}C]acetate during normal conditions ($n = 6$) or during reperfusion after 10 minutes of ischemia ($n = 5$). ^{13}C -Nuclear magnetic resonance spectra were acquired every 1 minute. Kinetic analysis of ^{13}C incorporation into GLU provided both tricarboxylic acid (TCA) cycle flux and the interconversion rate (F1) between the TCA cycle intermediate, alpha-ketoglutarate (alpha-KG), and the largely cytosolic GLU. The rate-pressure product in postischemic hearts was 46% of normal ($P < .05$). No difference in substrate utilization occurred between groups, with acetate accounting for 92% of the carbon units entering the TCA cycle at the citrate synthase step. TCA cycle flux in postischemic hearts was normal (normal hearts, 10.7 $\mu\text{mol}\cdot\text{min}^{-1}\cdot\text{g}^{-1}$; postischemic hearts, 9.4 $\mu\text{mol}\cdot\text{min}^{-1}\cdot\text{g}^{-1}$), whereas F1 was 72% lower at 2.9 \pm 0.4 versus 10.2 \pm 2.5 $\mu\text{mol}\cdot\text{min}^{-1}\cdot\text{g}^{-1}$ (mean \pm SE) in normal hearts ($P < .05$). From additional hearts perfused with 2.5 mmol/L [2- ^{13}C]acetate plus supplemental 5 mmol/L glucose, any potential differences in endogenous carbohydrate availability were proved not to account for the reduced rate alpha-KG and GLU exchange, which remained depressed in postischemic hearts. However, specific activities of the transaminase enzyme, catalyzing chemical exchange of alpha-KG and GLU, were the same, and transaminase flux was 100 $\mu\text{mol}\cdot\text{min}^{-1}\cdot\text{g}^{-1}$ in postischemic hearts versus 68 $\mu\text{mol}\cdot\text{min}^{-1}\cdot\text{g}^{-1}$ in normal hearts. Normal transaminase activity and the increased flux in postischemic hearts are contrary to the reduced F1. The findings indicate reduced metabolite transport rates across the mitochondrial membranes of stunned myocardium, particularly through the reversible alpha-KG-malate carrier.