Glucose is an Ineffective Substrate for Preservation of Machine Perfused Donor Hearts

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**Background:** Machine perfusion with oxygenated preservation solution can support donor heart metabolism but the preservation solution should contain an oxidizable substrate to improve cellular energetics. We hypothesized that myocardial metabolism can be influenced by exogenous substrates in the preservation solution.

**Methods:** Eight groups of isolated rat hearts ($n = 4$/group) were perfused with University of Wisconsin Machine Perfusion Solution containing carbon 13 ($^{13}$C) labeled glucose (2.5 mM, 5 mM, 10 mM, or 20 mM) or pyruvate (5 mM, 10 mM, 20 mM, or 40 mM). Hearts were perfused at 0.5 mL/min for 6 h at 8°C, and myocardial oxygen consumption ($\text{MVO}_2$) was measured. At end-perfusion, magnetic resonance spectroscopy was performed on ventricular extracts to determine the contribution of exogenous, labeled substrate to glycolysis and oxidative metabolism by $^{13}$C incorporation into metabolic intermediates.

**Results:** $\text{MVO}_2$ and perfusion conditions did not differ amongst groups. Exogenous glucose was metabolized by anaerobic glycolysis and contributed little to oxidative metabolism as measured by $^{13}$C incorporation into metabolic intermediates. Pyruvate led to greater lactate enrichment via the lactate dehydrogenase reaction. Enrichment of tricarboxylic acid (TCA) cycle intermediates was also greater in all pyruvate groups compared with glucose-containing groups ($P < 0.05$). Anaplerosis was increased in all pyruvate groups ($P < 0.05$).

**Conclusions:** The preservation solution substrate composition influences myocardial substrate metabolism during machine perfusion preservation of donor hearts. Exogenous glucose is a minor substrate in machine perfused myocardium, is primarily metabolized by glycolysis and does not contribute appreciably to oxidative metabolism. Pyruvate appears more effective in supporting myocardial metabolism. Further experiments examining the influences of substrate modifications on reperfusion function are warranted.

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