Journal of Medical Sciences at NEOMED
Volume 1, Issue 1, August 2022

Cardiac Metabolism in the Disease of Acute Myocardial Infarction

Nikhil Datla, MD[1]*, Chwen-Lih Chen, PhD[1], Patrick Kang, PhD[1], Yeong-Renn Chen, PhD[1], Takhar Kasumov, PhD[1], Serguei Ilchenko, PhD[1]

1. Northeast Ohio Medical University, College of Medicine, Rootstown, OH, 44272

** Corresponding author*

ABSTRACT

Overproduced reactive oxygen species (ROS) with decreased oxidative phosphorylation is a hallmark of the post-ischemic heart, which results in reperfusion-induced oxidative injury of the citric acid cycle (CAC). During ischemia, hypoxic conditions slow down the CAC resulting in succinate accumulation. Succinate is then rapidly oxidized during reperfusion, fueling ROS overproduction and contributing to ischemia-reperfusion (I/R) injury. We test the hypotheses that 1) reperfusion re-accelerates the CAC to correct succinate accumulation and 2) a vicious cycle caused by excess ROS can impair and downregulate the CAC plus other metabolic pathways in the post-ischemic heart. Nine–ten-week-old Sprague-Dawley rats (n=15) were subject to coronary ligation for 30-min followed by 24-h reperfusion. This process allowed us to closely mimic acute myocardial infarction (MI) and I/R injury. The non-ischemic and risk-regions of myocardium were excised, and the mitochondria were isolated. Dimethyl labeling was used to illuminate key metabolic pathways. Previous studies showed data that I/R impairs ADP-dependent O_2 consumption rate and ATP generation via downregulating CAC and fatty acid β-oxidation. However, a major finding in our study was that I/R dramatically upregulated the Phosphocreatine (PCr)/Creatine (Cr) shuttle ($p<0.05$) via upregulation of mitochondrial S-type creatine kinase (Ckmt2). The increased PCr formed in the mitochondria is transferred to the cytosol for ATP regeneration in-situ, which therefore increases the bioenergetic support of the post-ischemic myocardium. Therefore, we conclude that upregulating the PCr/Cr shuttle via increased Ckmt2 serves as feedback regulation of I/R, which can be useful for therapeutic intervention by increasing oxygenation and bioenergetics of the ischemic heart.